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USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus)near sequence) and (TCR and PCR) and (primer$3 and oligo$5)and beta	114	L8
USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus) and TCR and PCR) and (primer$3 and oligo$5)and beta	165	L7
USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus) and TCR and PCR) and (primer$3 or oligo$5)and beta	246	L6
USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus) and TCR and PCR) and (primer$3 or oligo$5)	267	L5
USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus) and TCR and PCR)	273	L4
USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus) near TCR)	3	L3
USPT,PGPB,JPAB,EPAB,DWPI	((degenerate or consensus) near TCR) and PCR	0	L2
USPT,PGPB,JPAB,EPAB,DWPI	(degenerate or consensus) near TCR near PCR near (primer or oligo$4)	0	L1

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L1          589 (PCR OR RTPCR) (P) (TCR OR (T CELL RECEPTOR?)) (P) (BETA) (P)
                (PRIMER? OR OLIGO OR OLIGOMER?)

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L3           27 L2 AND DEGENERATE

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L4            9 DUP REM L3 (18 DUPLICATES REMOVED)

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L4   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        1997:733370  CAPLUS
DOCUMENT NUMBER:         128:44336
TITLE:                   Human T cell receptor alpha and beta chain cDNA
                         amplification with a consensus primer
AUTHOR(S):               Moonka, Dilip K.; Loh, Elwyn Y.
CORPORATE SOURCE:        Department Medicine, Division Gastrointestinal
                         Diseases, University Pennsylvania Medical Center
                         Cancer Center, Philadelphia, PA, USA
SOURCE:                  Antigen T Cell Recept. (1997), 238-265.
                         Editor(s): Oksenberg, Jorge R.  Landes: Austin, Tex.
                         CODEN: 65HEAM
DOCUMENT TYPE:           Conference
LANGUAGE:                English
AB   The detn. of the variable and joining sequences of T
     cell receptors in different human T cell populations is
     of interest in many biol. contexts.  The use of reverse transcriptase to
     synthesize cDNA from mRNA followed by PCR has greatly
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facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific **primers** for the 5' end. This work describes a **degenerate**, consensus **primer** that binds to a relatively conserved area of the human .alpha. and .**beta**. **TCR** variable region.

SO Antigen T Cell Recept. (**1997**), 238-265. Editor(s): Oksenberg, Jorge R. Publisher: Landes, Austin, Tex.
CODEN: 65HEAM

AB The detn. of the variable and joining sequences of **T cell receptors** in different human T cell populations is of interest in many biol. contexts. The use of reverse transcriptase to synthesize cDNA from mRNA followed by **PCR** has greatly facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific **primers** for the 5' end. This work describes a **degenerate**, consensus **primer** that binds to a relatively conserved area of the human .alpha. and .**beta**. **TCR** variable region.

IT RT-**PCR** (reverse transcription-polymerase chain reaction) (human **T cell receptor** alpha and **beta** chain cDNA amplification with a consensus **primer**)

L4 ANSWER 2 OF 9 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 97205328 MEDLINE
DOCUMENT NUMBER: 97205328 PubMed ID: 9052832
TITLE: alpha, beta, gamma, and delta T cell antigen receptor genes arose early in vertebrate phylogeny.
AUTHOR: Rast J P; Anderson M K; Strong S J; Luer C; Litman R T; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: R37 AI23338 (NIAID)
SOURCE: IMMUNITY, **(1997 Jan)** 6 (1) 1-11.
Journal code: CCF; 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U75747; GENBANK-U75748; GENBANK-U75749; GENBANK-U75750; GENBANK-U75751; GENBANK-U75752; GENBANK-U75753; GENBANK-U75754; GENBANK-U75755; GENBANK-U75756; GENBANK-U75757; GENBANK-U75758; GENBANK-U75759; GENBANK-U75760; GENBANK-U75761; GENBANK-U75762; GENBANK-U75763; GENBANK-U75764; GENBANK-U75765; GENBANK-U75766; GENBANK-U75767; GENBANK-U75768; GENBANK-U75769; GENBANK-U75770; GENBANK-U75771; GENBANK-U75772; GENBANK-U75773; GENBANK-U75774; GENBANK-U75775; GENBANK-U75776; +
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970331

AB A series of products were amplified using a **PCR** strategy based on short minimally **degenerate primers** and R. eglanteria (clearnose skate) spleen cDNA as template. These products were used as probes to select corresponding cDNAs from a spleen cDNA library. The cDNA sequences exhibit significant identity with prototypic (alpha, **beta**, gamma, and delta T cell antigen receptor (**TCR**) genes. Characterization of cDNAs reveals extensive variable region diversity, putative diversity segments, and varying degrees of junctional diversification. This demonstrates expression of both alpha/**beta** and gamma/delta **TCR** genes at an early level of vertebrate phylogeny and indicates that the three major known classes of rearranging antigen receptors were present in the common ancestor of the present-day jawed vertebrates.

SO IMMUNITY, **(1997 Jan)** 6 (1) 1-11.
Journal code: CCF; 9432918. ISSN: 1074-7613.

AB A series of products were amplified using a **PCR** strategy based on short minimally **degenerate primers** and R. eglanteria (clearnose skate) spleen cDNA as template. These products were used as probes to select corresponding cDNAs from a spleen cDNA library. The cDNA sequences exhibit significant identity with prototypic (alpha, **beta**, gamma, and delta T cell antigen receptor (**TCR**) genes. Characterization of cDNAs reveals extensive variable region diversity, putative diversity segments, and varying degrees of junctional diversification. This demonstrates expression of both alpha/**beta** and gamma/delta **TCR** genes at an early level of vertebrate phylogeny and indicates that the three major known classes of rearranging antigen receptors. . .

L4 ANSWER 3 OF 9 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 96068761 MEDLINE
DOCUMENT NUMBER: 96068761 PubMed ID: 7579363
TITLE: Analysis of rearranged T-cell receptor beta-chain genes by polymerase chain reaction (PCR) DNA sequencing and automated high resolution PCR fragment analysis.
AUTHOR: Kneba M; Bolz I; Linke B; Hiddemann W
CORPORATE SOURCE: Department of Internal Medicine, Georg-August University, Goettingen, Germany.
SOURCE: BLOOD, **(1995 Nov 15)** 86 (10) 3930-7.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951219

AB Polymerase chain reaction (**PCR**)-directed amplification and sequencing of rearranged immune genes for identification of clone-specific markers are increasingly being used in acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma (NHL) patients instead of the time consuming and labor intensive Southern analysis. In previous reports, no single common V **beta** and J **beta** sequence had been identified that allowed reliable amplification of the majority of rearranged T-cell antigen receptor (**TCR**)-**beta** V-D-J junctions at the DNA level because of the relatively large number of possible **TCR**-**beta** variable (V **beta**) and joining (J **beta**) gene segments involved in the rearrangement processes. In the present study we designed highly **degenerate PCR primers** directed against conserved sequences of the J **beta**

genes. IN combination with a previously published consensus V **beta primer**, these J **beta primers** specifically amplify **TCR- beta** V-N(D)N-J junctions from genomic DNA. Using this approach we studied DNA extracted from biopsy material of nine patients with T-cell lymphoproliferative disorders, one c-ALL patient, and five patients with nonmalignant diseases. T-cell lines Molt 3, Jurkat, and HM 2 served as monoclonal controls. Individual **PCR** products were sequenced after cloning. The nucleotide sequences of 96 randomly chosen recombinant vectors were determined. In the polyclonal controls all analyzed clones differed in their **TCR-beta** V-N(D)N-J junctions. In the T-cell lines, in all of the T-cell malignancies, and in the c-ALL, monoclonal **PCR** products could be identified by demonstration of clonally restricted V-N(D)N-J junctions. The **PCR** results were confirmed by automated fluorescence quantification and size determination of **PCR** products after separation in a high-resolution polyacrylamide gel. The procedure allows rapid and specific characterization of clonal **TCR-beta** rearrangements from genomic DNA and will significantly simplify current experimental approaches to identify and to quantitate malignant T cells during initial staging and follow-up of T-lineage NHL and ALL patients.

SO BLOOD, **(1995 Nov 15)** 86 (10) 3930-7.
Journal code: A8G; 7603509. ISSN: 0006-4971.

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L4 ANSWER 4 OF 9 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 95369847 MEDLINE
DOCUMENT NUMBER: 95369847 PubMed ID: 7642232
TITLE: Identification and characterization of T-cell antigen receptor-related genes in phylogenetically diverse vertebrate species.
AUTHOR: Rast J P; Haire R N; Litman R T; Pross S; Litman G W
CORPORATE SOURCE: University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: RO1AI23338 (NIAID)
SOURCE: IMMUNOGENETICS, **(1995)** 42 (3) 204-12.
Journal code: GI4; 0420404. ISSN: 0093-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U22666; GENBANK-U22667; GENBANK-U22668; GENBANK-U22669; GENBANK-U22670; GENBANK-U22671; GENBANK-U22672; GENBANK-U22673; GENBANK-U22674; GENBANK-U22675; GENBANK-U22676; GENBANK-U22677; GENBANK-U22678; GENBANK-U22679; GENBANK-U23067
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19950930
Entered Medline: 19950920

AB Characterization of the structure, multiplicity, organization, and cell lineage-specific expression of **T-cell receptor** (**TCR**) genes of nonmammalian vertebrate species is central to the understanding of the evolutionary origins of rearranging genes of the vertebrate immune system. We recently described a polymerase chain reaction (**PCR**) strategy that relies on short sequence similarities shared by nearly all vertebrate **TCR** and immunoglobulin (Ig) variable (V) regions and have used this approach to isolate a **TCR beta** (TCRB) homolog from a cartilaginous fish. Using these short **PCR** products as probes in spleen cDNA and genomic libraries, we were able to isolate a variety of unique **TCR** and **TCR**-like genes. Here we report the identification and characterization of a chicken **TCR** gamma (TCRG) homolog, apparent Xenopus and pufferfish **TCR** alpha (TCRA) homologs, and two horned shark **TCR** delta (TCRD)-like genes. In addition, we have identified what could be a novel representative of the Ig gene superfamily in the pufferfish. This method of using short, minimally **degenerate PCR primers** should speed progress in the phylogenetic investigations of the **TCR** and related genes and lend important insights into both the origins and functions of these unique gene systems.

SO IMMUNOGENETICS, **(1995)** 42 (3) 204-12.
Journal code: GI4; 0420404. ISSN: 0093-7711.

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L4 ANSWER 5 OF 9 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 95023888 MEDLINE
DOCUMENT NUMBER: 95023888 PubMed ID: 7937749
TITLE: T-cell receptor gene homologs are present in the most primitive jawed vertebrates.
AUTHOR: Rast J P; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701.
CONTRACT NUMBER: AI-23338 (NIAID)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1994 Sep 27)** 91 (20) 9248-52.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U07622; GENBANK-U07623; GENBANK-U07624; GENBANK-U09531; GENBANK-U09532; GENBANK-U09533; GENBANK-U09534
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19960129
Entered Medline: 19941027

AB The phylogenetic origins of T-cell immunity and T-cell antigen receptor (**TCR**) genes have not been established. A **PCR** approach using short, minimally **degenerate** oligodeoxynucleotide **primers** complementing conserved variable region segments amplifies **TCR**-like products from the genomic DNA of Heterodontus francisci (horned shark), a representative phylogenetically primitive cartilaginous fish. One of these products has been used as a probe to screen a Heterodontus spleen cDNA library and a clone was identified that is most related at the nucleotide sequence and predicted peptide levels to higher vertebrate **TCR beta**-chain genes. Genomic analyses of the **TCR** homologs indicate that recombining variable and joining region segments as well as constant region exons are encoded by extensive gene families, organized in the multicluster form, characteristic of both the immunoglobulin heavy- and light-chain gene loci in the cartilaginous fishes. Greater numbers of homologous products were identified when a probe complementing the putative constant region of the **TCR** homolog was used to screen the same cDNA library. A high degree of intergenic variation is associated with the putative variable region segments of these isolates. Direct evidence is presented for **TCR** -like genes, which presumably are associated with T-cell function, at the earliest stages in the phylogenetic emergence of jawed vertebrates.

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1994 Sep 27)** 91 (20) 9248-52.
Journal code: PV3; 7505876. ISSN: 0027-8424.

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L4 ANSWER 6 OF 9 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 94179857 MEDLINE
DOCUMENT NUMBER: 94179857 PubMed ID: 7510755
TITLE: A consensus primer to amplify both alpha and beta chains of the human T cell receptor.
AUTHOR: Moonka D; Loh E Y
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania Medical Center, Philadelphia.
CONTRACT NUMBER: AI33214 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, **(1994 Feb 28)** 169 (1) 41-51.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19960129
Entered Medline: 19940418

AB The use of reverse transcriptase in conjunction with the polymerase chain reaction (RT-**PCR**) has proven invaluable in the analysis of the **T cell receptor** (**TCR**) repertoire of different populations of T cells. However, the presence of a variable region in the **T cell receptor** has hindered the design of **primers** for the 5' end of the **TCR** cDNA. We describe the design and use of a **degenerate** consensus **primer** that allows amplification of both the alpha and **beta** chains of the human **TCR**. We have used this **primer** in the analysis of the **TCR** distribution of T cell clones, peripheral blood lymphocytes and lymphocytes residing in tissue.

In addition, the **primer** has allowed the identification of an alternative splice site in the **beta** chain constant region which cannot translate into a functional constant region. We have found the **primer** to be easy to use, sensitive and specific.

SO JOURNAL OF IMMUNOLOGICAL METHODS, **(1994 Feb 28)** 169 (1) 41-51. Journal code: IFE; 1305440. ISSN: 0022-1759.

AB The use of reverse transcriptase in conjunction with the polymerase chain reaction (RT-**PCR**) has proven invaluable in the analysis of the **T cell receptor (TCR)** repertoire of different populations of T cells. However, the presence of a variable region in the **T cell receptor** has hindered the design of **primers** for the 5' end of the **TCR** cDNA. We describe the design and use of a **degenerate** consensus **primer** that allows amplification of both the alpha and **beta** chains of the human **TCR**. We have used this **primer** in the analysis of the **TCR** distribution of T cell clones, peripheral blood lymphocytes and lymphocytes residing in tissue. In addition, the **primer** has allowed the identification of an alternative splice site in the **beta** chain constant region which cannot translate into a functional constant region. We have found the **primer** to be easy to use, sensitive and specific.

L4 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:270260 BIOSIS
DOCUMENT NUMBER: PREV199396000485
TITLE: Molecular cloning of major histocompatibility complex class I cDNAs from Atlantic salmon (Salmo salar.
AUTHOR(S): Grimholt, Unni Vvar Hordvik (1); Fosse, Viggo M.; Olsaker, Ingrid; Endresen, Curt; Lie, Oystein
CORPORATE SOURCE: (1) Dep. Animal Genetics, Norwegian College of Vet. Med., P.O. Box 8146 Dep., N-0033 Oslo 1 Norway
SOURCE: Immunogenetics, (1993) Vol. 37, No. 6, pp. 469-473. ISSN: 0093-7711.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The major histocompatibility complex (Mhc) has attracted much attention because of its immense polymorphism, its importance in transplantation, and its indisputable role in disease susceptibility in humans (Chen and Parham 1989; Hill et al. 1991) and in animals (Lie 1990). Previously, typical Mhc features reflected in allograft rejection and mixed leucocyte reactivity were the only indications that an Mhc also existed in teleost fish (Stet and Egberts 1991). The use of polymerase chain reaction (**PCR**) with **degenerate** oligonucleotides from conserved Mhc regions provided the first direct evidence for Mhc class I and class II genes in a fish, the teleost carp (Hashimoto et al. 1990). The primary aim of our study was to isolate and characterize expressed Mhc molecules in Atlantic salmon, and thereby provide data for further studies on evolutionary and disease aspects of the Mhc and its polymorphism. An atlantic salmon-specific Mhc probe from leucocyte RNA was generated by **PCR** based on **primers** from conserved regions of known Mhc genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik and co-workers (this issue). This salmon-specific probe was employed to screen a leucocyte lambda-gt10 cDNA library based on a few individuals, from which Mhc-positive cDNAs were derived. The cDNAs analyzed in this report were established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal **primers**, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using the UWGCG software (Devereux et al. 1984). The FASTA program (Pearson and Lipman 1988) was used to search the EMBL database. In accordance with the nomenclature proposed by Klein and co-workers (1990), we adopted the designation Mhc-Sasa, as proposed by Stet and Egberts (1991), for the two partial Atlantic salmon (Salmo salar) Mhc nucleotide sequences which we aligned to the EMBL database. One of these clones, p18, shared sequence similarity to Mhc class II molecules (Hordvik et al., this issue). The other clone, p23 (1.8 kilobase (kb)), showed sequence similarity to Mhc class I sequences with a non-translated tail of 1200 nucleotides (nt) and an open reading frame (orf) of 190 aminoacids (aa) starting in the middle of the alpha-2 domain (Fig. 1). The latter cDNA clone was used in a second screening of the cDNA library, which resulted in a potential full-length clone, Sasa p30 (2.8 kb), with an orf corresponding to 343 aa and a nontranslated tail of 1800 nt (Fig. 1). The domain boundaries of Sasa p30 were assigned by alignment with other Mhc class I molecule (Fig. 2). The aa sequence similarities between Sasa and Xenopua, and lizard, man, mouse, chicken, and carp are striking, and support the hypothesis that the isolated cDNA clones encode salmon Mhc class I molecules. Both and cysteines forming intrachain disulphide bonds within the alpha-2 and alpha-3 domains, and the potential glycosylation site at N-84 (numbering is based on the salmon sequence), are conserved. In the putative Sasa p30 transmembrane region there is a stretch of 21 hydrophobic residues flanked on both sides by hydrophilic segments, indicating a membrane anchored protein. Most of the residues assumed to be directly involved in the structure of the alpha-3 domain are conserved in the salmon sequence (C-198, F-203, Y-204, P-205, W-212, G-234, Y-254, C-256, and V-258; Williams et al. 1987). Nine residues pointing into the antigenic recognition site, and probably involved in recognizing constant features on processed antigens, are conserved in the alpha-1 and alpha-2 domains of humans and mice (Bjorkman et al. 1987). These residues are also conserved in the salmon sequence (L-5, Y-7, F-21, G-25, Y-57, T-140, K-143, Y-157, and Y-169). The signal peptide may be incomplete, as the cDNA clone started with a methionine residue. Both cDNA clones contained 17 repeated CA dinucleotides 110 nt after the first stop codon. This repeated sequence is polymorphic (data will be presented elsewhere), and can be used as an Mhc-linked marker. The two Sasa clones, p23 and p30, differed by 24 nt representing 14 aa residues (Fig. 1). Eleven of the variable aa positions resided in the alpha-2 helical domain and only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human **T-cell receptor** interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only one substitution corresponded to a human, polymorphic, peptide-binding residue (res. 154). It is not possible to determine from our data whether the p23 and p30 cDNA clones are alleles or originate from different genes (isotypes). However, the clustering of replacement substitutions in the alpha-2 region, and the fact that the library from which the cDNA clones were selected was derived from several individuals, supports the hypothesis that the observed variation is attributable to allelism. An amino acid comparison between the salmon alpha domains and those of carp, chicken, HLA-A, H-2K, and lizard showed the significantly lowest similarity to carp (p lt 0.05). The low similarity between salmon and carp is also reflected in the phylogenetic tree (Fig. 3) based on the

membrane-proximal aa sequences of Mhc class I (alpha-3) and class II (alpha-2 and **beta**-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is jointed to the H-2K/HLA-A node, but this is a doubtful result. Similarly, the evolutionary relationship between carp, Xenopus, and shark class I sequences are uncertain, and more Mhc class I sequences from lower vertebrates are needed to clarify the picture. All the class II sequences reside on the same branch. Shark class II is joined to a human class II alpha sequence, and the trout and salmon class II peptides are very similar and branched together with carp **beta**-2. Hashimoto and co-workers (1990) used **degenerate primers** directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast to the carp class II sequence, originates from a pseudogene and has thus acquired a considerable number of mutations. The carp class I sequence could also represent a nonclassical carp Mhc molecule. Both suggestions would explain why the carp class I sequence has the lowest overall alpha domain aa similarity (20%) to salmon. Further speculation on teleostean evolution must be deferred until further information is available on expressed carp Mhc class I sequences. A FASTA search with the p30 cDNA sequence identified 40 Mhc class I sequences as being most similar to the salmon sequence. These sequences included both nonclassical (mouse Q7(b), mouse T1a(c), and human HLA-G (HLA 6.0)) and classical Mhc class I genes. The question as to whether Atlantic salmon has both classical and nonclassical homologues, as seen in human and mouse, will be possible to answer when more Sasa loci have been identified. In conclusion, this study, together with the work done by Hordvik and co-workers (this issue), demonstrates the existence of expressed Mhc class I and class II molecules in Atlantic salmon. The clonal variation seen in these reports indicates allelic polymorphism as seen in other species, but the number of alleles and loci involved remains to be established. The teleost class II **beta**-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides is unclear. Further information on expressed carp class I sequences is needed to resolve this.

SO Immunogenetics, (1993) Vol. 37, No. 6, pp. 469-473.
ISSN: 0093-7711.

AB . . only indications that an Mhc also existed in teleost fish (Stet and Egberts 1991). The use of polymerase chain reaction (**PCR**) with **degenerate** oligonucleotides from conserved Mhc regions provided the first direct evidence for Mhc class I and class II genes in a. . . and disease aspects of the Mhc and its polymorphism. An atlantic salmon-specific Mhc probe from leucocyte RNA was generated by **PCR** based on **primers** from conserved regions of known Mhc genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik. . . established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal **primers**, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using. . . only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human **T-cell receptor** interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only. . . phylogenetic tree (Fig. 3) based on the membrane-proximal aa sequences of Mhc class I (alpha-3) and class II (alpha-2 and **beta**-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is jointed. . . class II alpha sequence, and the trout and salmon class II peptides are very similar and branched together with carp **beta**-2. Hashimoto and co-workers (1990) used **degenerate primers** directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast. . . seen in other species, but the number of alleles and loci involved remains to be established. The teleost class II **beta**-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides. . .

L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:606319 CAPLUS
DOCUMENT NUMBER: 117:206319
TITLE: Identification of cell subpopulations using modified PCR to amplify DNA encoding proteins with constant and variable regions
INVENTOR(S): Danska, Jayne S.; Fathman, Garrison C.
PATENT ASSIGNEE(S): Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9119816	A1	19911226	WO 1991-US4317	19910617 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2086015	AA	19911221	CA 1991-2086015	19910617 <--

PRIORITY APPLN. INFO.: US 1990-541123 19900620

AB A method for amplifying DNA encoding a protein having a const. and variable region by a polymerase chain reaction (**PCR**) modification is described. The method employs 2 **primers**, one of which is complementary to a const. region. The other is a **degenerate primer** complementary to a portion of the DNA encoding a consensus sequence. The amplified DNA can be cloned and sequenced, so that the cells expressing the protein can be identified. The resulting information can be used to design therapies for autoimmune diseases, lymphomas, and leukemias (no data). This procedure was applied to amplification, cloning, and sequencing of mouse **T-cell receptor** .alpha. and .**beta**. cDNA fragments comprising V and J regions.

PI WO 9119816 A1 **19911226**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9119816	A1	19911226	WO 1991-US4317	19910617 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2086015	AA	19911221	CA 1991-2086015	19910617 <--

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degenerate primer complementary to a portion of the DNA encoding a consensus sequence. The amplified DNA can be cloned and sequenced, so that the cells expressing the protein can be identified. The resulting information can be used to design therapies for autoimmune diseases, lymphomas, and leukemias (no data). This procedure was applied to amplification, cloning, and sequencing of mouse **T-cell receptor** .alpha. and .**beta**. cDNA fragments comprising V and J regions.

L4 ANSWER 9 OF 9 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 91184261 MEDLINE
DOCUMENT NUMBER: 91184261 PubMed ID: 2009906
TITLE: Conserved nucleotide sequences at the 5' end of T cell receptor variable genes facilitate polymerase chain reaction amplification.
AUTHOR: Broeren C P; Verjans G M; Van Eden W; Kusters J G; Lenstra J A; Logtenberg T
CORPORATE SOURCE: Institute of Infectious Diseases and Immunology, School of Veterinary Medicine, University of Utrecht, The Netherlands.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, **(1991 Mar)** 21 (3) 569-75.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19910526
Entered Medline: 19910503
AB Alignment of all available nucleotide sequences of mouse and rat alpha/**beta T cell receptor** (**TcR**) variable (V) regions revealed the presence of relatively conserved sequences at the 5' end of the V gene segments. Based on these conserved sequences, **degenerate primers** were developed for use in the polymerase chain reaction (**PCR**). The **degenerate primers** developed on the basis of the conserved sequences at the 5' end of rat and mouse V gene segments are expected to enable the amplification of all mouse and rat **TcR** alpha/**beta** chain V regions. To test their applicability, the **primers** were used for the amplification of the V region of the **TcR** alpha/**beta** expressed by rat T cell lines. After amplification, the **TcR** V regions expressed were cloned and sequenced. The Z1a T cell line was shown to use the same **TcR** V gene segments (V alpha 2 and V **beta** 8.2), as most other experimental allergic encephalomyelitis associated T cell lines, but had different D and J segments. In spite of these differences at the nucleotide level, a remarkable conservation of the amino acid sequence at the V **beta** D **beta** J **beta** junction was found. Alignment of a large number of human V alpha and V **beta** gene segments revealed the presence of similarly conserved sequences. **Degenerate primers** based on these conserved sequences enabled the amplification of **TcR** V regions of human T cell lines.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1991 Mar)** 21 (3) 569-75.
Journal code: EN5; 1273201. ISSN: 0014-2980.
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```
=> dis his

     (FILE 'HOME' ENTERED AT 17:22:59 ON 29 AUG 2001)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:23:11 ON 29 AUG 2001
L1          589 S (PCR OR RTPCR) (P) (TCR OR (T CELL RECEPTOR?)) (P) (BETA) (P)
L2          495 S L1 AND PY < 1998
L3           27 S L2 AND DEGENERATE
L4            9 DUP REM L3 (18 DUPLICATES REMOVED)

=> s l1 and degenerate
L5          34 L1 AND DEGENERATE

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           13 DUP REM L5 (21 DUPLICATES REMOVED)

=> dis l6 1-13 ibib abs kwic
```

L6 ANSWER 1 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001099135 MEDLINE
DOCUMENT NUMBER: 20565479 PubMed ID: 11113282
TITLE: T-cell antigen receptors in Atlantic cod (Gadus morhua l.): structure, organisation and expression of TCR alpha and beta genes.
AUTHOR: Wermenstam N E; Pilstrom L
CORPORATE SOURCE: Immunology Programme, Department of Cell and Molecular Biology, BMC, Uppsala University, Box 596, S-751 24, Uppsala, Sweden.
SOURCE: DEVELOPMENTAL AND COMPARATIVE IMMUNOLOGY, (2001 Mar) 25 (2) 117-35.

Journal code: E3M. ISSN: 0145-305X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ133844; GENBANK-AJ133845; GENBANK-AJ133846; GENBANK-AJ133847; GENBANK-AJ133848; GENBANK-AJ133849; GENBANK-AJ133850; GENBANK-AJ133851
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and constant region segments for **PCR**, we were able to isolate putative TCRalpha and **beta** chain full length cDNAs in Atlantic cod. The Valpha and Vbeta domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The Jalpha and Jbeta region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and immunoglobulin light chain J regions. Similar to other vertebrates, the Atlantic cod Calpha and Cbeta sequences exhibit distinct immunoglobulin, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod Cbeta sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerisation and cell surface expression are observed. Four different cod Cbeta sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of Cbeta. Based on Southern blot analyses, the TCRalpha and **beta** gene loci appear to be arranged in translocon organisation (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the TCRalpha and **beta** chains in thymus, spleen and head kidney, expression of the TCRbeta chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.
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L6 ANSWER 2 OF 13 MEDLINE
ACCESSION NUMBER: 2000411646 MEDLINE
DOCUMENT NUMBER: 20394656 PubMed ID: 10938743
TITLE: Immunopurification of T-cells from sea bass Dicentrarchus labrax (L.).
AUTHOR: Scapigliati G; Romano N; Abelli L; Meloni S; Ficca A G; Buonocore F; Bird S; Secombes C J
CORPORATE SOURCE: Dipartimento di Scienze Ambientali, Universita della Tuscia, Viterbo, Italy.. scapigg@unitus.it
SOURCE: FISH & SHELLFISH IMMUNOLOGY, (2000 May) 10 (4) 329-41.
Journal code: DR8; 9505220. ISSN: 1050-4648.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829

AB The monoclonal antibody DLT15, specific for thymocytes and peripheral T-cells of the teleost fish Dicentrarchus labrax (sea bass), was used to purify immunoreactive cells from blood and gut-associated lymphoid tissue. The purification was performed by immuno-magnetic sorting of leucocyte fractions enriched by Percoll density gradient centrifugation, and the purity of the isolated cells was estimated by cytofluorimetric analysis. Following a single step, the percentage of DLT15-purified cells was 88 +/- 10% for gut-associated lymphoid tissue and 79 +/- 18% for blood leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-**PCR** experiments using as **primers degenerate** oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout **TcR beta** chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV **beta** 3. By 3'-RACE the cDNA was elongated to obtain the **TcR** constant region, with high similarity to other fish **TcR** sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.
AB . . . +/- 18% for blood leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-**PCR** experiments using as **primers degenerate** oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout **TcR beta** chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV **beta** 3. By 3'-RACE the cDNA was elongated to obtain the **TcR** constant region, with high similarity to other fish **TcR** sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.

L6 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:853499 CAPLUS
TITLE: T-cell antigen receptors in Atlantic cod (Gadus morhua L.): structure, organisation and expression of TCR .alpha. and .beta. genes
AUTHOR(S): Wermenstam, N. E.; Pilstrom, L.
CORPORATE SOURCE: BMC, Department of Cell and Molecular Biology, Immunology Programme, Uppsala University, Uppsala,

S-751 24, Swed.
SOURCE: Dev. Comp. Immunol. (2000), 25(2), 117-135
CODEN: DCIMDQ; ISSN: 0145-305X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and const. region segments for **PCR**, we were able to isolate putative **TCR**.alpha. and .**beta**. chain full length cDNAs in Atlantic cod. The V.alpha. and V.**beta**. domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.**beta**. region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.**beta**. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.**beta**. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are obsd. Four different cod C.**beta**. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.**beta**.. Based on Southern blot analyses, the **TCR**.alpha. and .**beta**. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the **TCR** .alpha. and .**beta**. chains in thymus, spleen and head kidney, expression of the **TCR**.**beta**. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.
REFERENCE COUNT: 57
REFERENCE(S): (2) Alcover, A; J Biol Chem 1990, V265, P4131 CAPLUS
(3) Arnaud, J; Int Immunol 1997, V9, P615 CAPLUS
(5) Backstrom, B; Science 1998, V281, P835 CAPLUS
(6) Bengten, E; Dev Comp Immunol 1994, V18, P109 CAPLUS
(7) Bengten, E; Eur J Immunol 1991, V21, P3027 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and const. region segments for **PCR**, we were able to isolate putative **TCR**.alpha. and .**beta**. chain full length cDNAs in Atlantic cod. The V.alpha. and V.**beta**. domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.**beta**. region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.**beta**. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.**beta**. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are obsd. Four different cod C.**beta**. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.**beta**.. Based on Southern blot analyses, the **TCR**.alpha. and .**beta**. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the **TCR** .alpha. and .**beta**. chains in thymus, spleen and head kidney, expression of the **TCR**.**beta**. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
ACCESSION NUMBER: 1999:605448 CAPLUS
DOCUMENT NUMBER: 132:149888
TITLE: Rearranged T lymphocyte antigen receptor genes as markers of malignant T cells
AUTHOR(S): Dreitz, M. J.; Ogilvie, G.; Kee Sim, G.
CORPORATE SOURCE: HESKA Corporation, Ft. Collins, CO, USA
SOURCE: Vet. Immunol. Immunopathol. (1999), 69(2-4), 113-119
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have recently cloned a no. of canine **T cell receptor** (**TCR**) V.**beta**. genes using **degenerate** oligonucleotides. From the DNA sequences of the resulting clones and the canine V.**beta**. gene sequences in the literature, seven distinct canine **TCR** V.**beta**. genes were identified. V.**beta**. specific **PCR primers** were designed for each of the seven **TCR** V.**beta**. genes such that under defined conditions, each **primer** could only amplify a specific **TCR** V.**beta**. gene in conjunction with the same 3' const. region (C.**beta**.) **primer**. By performing RT-**PCR** on RNA derived from a source contg. T lymphocytes, the presence and expansion of T cells expressing a particular V.**beta**. gene could be detected. Moreover, the clonality or diversity of a T cell population under anal. could be easily detd. by the VDJ junctional sequence of the amplified V.**beta**. **PCR** product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.
REFERENCE COUNT: 10
REFERENCE(S): (2) Davis, M; Nature 1988, V334, P395 CAPLUS
(3) Hood, L; Cell 1985, V40, P225 CAPLUS
(4) Ito, K; Immunogenetics 1993, V38, P60 CAPLUS
(5) Malissen, M; Cell 1984, V37, P1101 CAPLUS
(6) Patten, P; Nature 1984, V312, P40 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB We have recently cloned a no. of canine **T cell receptor** (**TCR**) V.**beta**. genes using **degenerate** oligonucleotides. From the DNA sequences of the resulting clones and the canine V.**beta**. gene sequences in the literature, seven distinct canine **TCR** V.**beta**. genes were identified. V.**beta**. specific **PCR primers**

were designed for each of the seven TCR V.beta. genes such that under defined conditions, each primer could only amplify a specific TCR V.beta. gene in conjunction with the same 3' const. region (C.beta.) primer. By performing RT-PCR on RNA derived from a source contg. T lymphocytes, the presence and expansion of T cells expressing a particular V.beta. gene could be detected. Moreover, the clonality or diversity of a T cell population under anal. could be easily detd. by the VDJ junctional sequence of the amplified V.beta. PCR product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.

L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:733370 CAPLUS
DOCUMENT NUMBER: 128:44336
TITLE: Human T cell receptor alpha and beta chain cDNA amplification with a consensus primer
AUTHOR(S): Moonka, Dilip K.; Loh, Elwyn Y.
CORPORATE SOURCE: Department Medicine, Division Gastrointestinal Diseases, University Pennsylvania Medical Center Cancer Center, Philadelphia, PA, USA
SOURCE: Antigen T Cell Recept. (1997), 238-265. Editor(s): Oksenberg, Jorge R. Landes: Austin, Tex. CODEN: 65HEAM
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The detn. of the variable and joining sequences of T cell receptors in different human T cell populations is of interest in many biol. contexts. The use of reverse transcriptase to synthesize cDNA from mRNA followed by PCR has greatly facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific primers for the 5' end. This work describes a degenerate, consensus primer that binds to a relatively conserved area of the human .alpha. and .beta. TCR variable region.
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IT RT-PCR (reverse transcription-polymerase chain reaction) (human T cell receptor alpha and beta chain cDNA amplification with a consensus primer)

L6 ANSWER 6 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97205328 MEDLINE
DOCUMENT NUMBER: 97205328 PubMed ID: 9052832
TITLE: alpha, beta, gamma, and delta T cell antigen receptor genes arose early in vertebrate phylogeny.
AUTHOR: Rast J P; Anderson M K; Strong S J; Luer C; Litman R T; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: R37 AI23338 (NIAID)
SOURCE: IMMUNITY, (1997 Jan) 6 (1) 1-11. Journal code: CCF; 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U75747; GENBANK-U75748; GENBANK-U75749; GENBANK-U75750; GENBANK-U75751; GENBANK-U75752; GENBANK-U75753; GENBANK-U75754; GENBANK-U75755; GENBANK-U75756; GENBANK-U75757; GENBANK-U75758; GENBANK-U75759; GENBANK-U75760; GENBANK-U75761; GENBANK-U75762; GENBANK-U75763; GENBANK-U75764; GENBANK-U75765; GENBANK-U75766; GENBANK-U75767; GENBANK-U75768; GENBANK-U75769; GENBANK-U75770; GENBANK-U75771; GENBANK-U75772; GENBANK-U75773; GENBANK-U75774; GENBANK-U75775; GENBANK-U75776; +
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970331
AB A series of products were amplified using a PCR strategy based on short minimally degenerate primers and R. eglanteria (clearnose skate) spleen cDNA as template. These products were used as probes to select corresponding cDNAs from a spleen cDNA library. The cDNA sequences exhibit significant identity with prototypic (alpha, beta, gamma, and delta T cell antigen receptor (TCR) genes. Characterization of cDNAs reveals extensive variable region diversity, putative diversity segments, and varying degrees of junctional diversification. This demonstrates expression of both alpha/beta and gamma/delta TCR genes at an early level of vertebrate phylogeny and indicates that the three major known classes of rearranging antigen receptors were present in the common ancestor of the present-day jawed vertebrates.
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L6 ANSWER 7 OF 13 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96068761 MEDLINE
DOCUMENT NUMBER: 96068761 PubMed ID: 7579363
TITLE: Analysis of rearranged T-cell receptor beta-chain genes by polymerase chain reaction (PCR) DNA sequencing and automated high resolution PCR fragment analysis.

AUTHOR: Kneba M; Bolz I; Linke B; Hiddemann W
CORPORATE SOURCE: Department of Internal Medicine, Georg-August University, Goettingen, Germany.
SOURCE: BLOOD, (1995 Nov 15) 86 (10) 3930-7.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951219

AB Polymerase chain reaction (**PCR**)-directed amplification and sequencing of rearranged immune genes for identification of clone-specific markers are increasingly being used in acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma (NHL) patients instead of the time consuming and labor intensive Southern analysis. In previous reports, no single common V **beta** and J **beta** sequence had been identified that allowed reliable amplification of the majority of rearranged T-cell antigen receptor (**TCR**)-**beta** V-D-J junctions at the DNA level because of the relatively large number of possible **TCR-beta** variable (V **beta**) and joining (J **beta**) gene segments involved in the rearrangement processes. In the present study we designed highly **degenerate PCR primers** directed against conserved sequences of the J **beta** genes. IN combination with a previously published consensus V **beta primer**, these J **beta primers** specifically amplify **TCR- beta** V-N(D)N-J junctions from genomic DNA. Using this approach we studied DNA extracted from biopsy material of nine patients with T-cell lymphoproliferative disorders, one c-ALL patient, and five patients with nonmalignant diseases. T-cell lines Molt 3, Jurkat, and HM 2 served as monoclonal controls. Individual **PCR** products were sequenced after cloning. The nucleotide sequences of 96 randomly chosen recombinant vectors were determined. In the polyclonal controls all analyzed clones differed in their **TCR-beta** V-N(D)N-J junctions. In the T-cell lines, in all of the T-cell malignancies, and in the c-ALL, monoclonal **PCR** products could be identified by demonstration of clonally restricted V-N(D)N-J junctions. The **PCR** results were confirmed by automated fluorescence quantification and size determination of **PCR** products after separation in a high-resolution polyacrylamide gel. The procedure allows rapid and specific characterization of clonal **TCR-beta** rearrangements from genomic DNA and will significantly simplify current experimental approaches to identify and to quantitate malignant T cells during initial staging and follow-up of T-lineage NHL and ALL patients.

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L6 ANSWER 8 OF 13 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 95369847 MEDLINE
DOCUMENT NUMBER: 95369847 PubMed ID: 7642232
TITLE: Identification and characterization of T-cell antigen receptor-related genes in phylogenetically diverse vertebrate species.
AUTHOR: Rast J P; Haire R N; Litman R T; Pross S; Litman G W
CORPORATE SOURCE: University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: RO1AI23338 (NIAID)
SOURCE: IMMUNOGENETICS, (1995) 42 (3) 204-12.
Journal code: GI4; 0420404. ISSN: 0093-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U22666; GENBANK-U22667; GENBANK-U22668; GENBANK-U22669; GENBANK-U22670; GENBANK-U22671; GENBANK-U22672; GENBANK-U22673; GENBANK-U22674; GENBANK-U22675; GENBANK-U22676; GENBANK-U22677; GENBANK-U22678; GENBANK-U22679; GENBANK-U23067
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19950930
Entered Medline: 19950920

AB Characterization of the structure, multiplicity, organization, and cell lineage-specific expression of **T-cell receptor** (**TCR**) genes of nonmammalian vertebrate species is central to the understanding of the evolutionary origins of rearranging genes of the vertebrate immune system. We recently described a polymerase chain reaction (**PCR**) strategy that relies on short sequence similarities shared by nearly all vertebrate **TCR** and immunoglobulin (Ig) variable (V) regions and have used this approach to

isolate a **TCR beta** (TCRB) homolog from a cartilaginous fish. Using these short **PCR** products as probes in spleen cDNA and genomic libraries, we were able to isolate a variety of unique **TCR** and **TCR**-like genes. Here we report the identification and characterization of a chicken **TCR** gamma (TCRG) homolog, apparent Xenopus and pufferfish **TCR** alpha (TCRA) homologs, and two horned shark **TCR** delta (TCRD)-like genes. In addition, we have identified what could be a novel representative of the Ig gene superfamily in the pufferfish. This method of using short, minimally **degenerate PCR primers** should speed progress in the phylogenetic investigations of the **TCR** and related genes and lend important insights into both the origins and functions of these unique gene systems.

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L6 ANSWER 9 OF 13 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 95023888 MEDLINE
DOCUMENT NUMBER: 95023888 PubMed ID: 7937749
TITLE: T-cell receptor gene homologs are present in the most primitive jawed vertebrates.
AUTHOR: Rast J P; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701.
CONTRACT NUMBER: AI-23338 (NIAID)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Sep 27) 91 (20) 9248-52. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U07622; GENBANK-U07623; GENBANK-U07624; GENBANK-U09531; GENBANK-U09532; GENBANK-U09533; GENBANK-U09534
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19960129
Entered Medline: 19941027

AB The phylogenetic origins of T-cell immunity and T-cell antigen receptor (**TCR**) genes have not been established. A **PCR** approach using short, minimally **degenerate** oligodeoxynucleotide **primers** complementing conserved variable region segments amplifies **TCR**-like products from the genomic DNA of Heterodontus francisci (horned shark), a representative phylogenetically primitive cartilaginous fish. One of these products has been used as a probe to screen a Heterodontus spleen cDNA library and a clone was identified that is most related at the nucleotide sequence and predicted peptide levels to higher vertebrate **TCR beta**-chain genes. Genomic analyses of the **TCR** homologs indicate that recombining variable and joining region segments as well as constant region exons are encoded by extensive gene families, organized in the multicluster form, characteristic of both the immunoglobulin heavy- and light-chain gene loci in the cartilaginous fishes. Greater numbers of homologous products were identified when a probe complementing the putative constant region of the **TCR** homolog was used to screen the same cDNA library. A high degree of intergenic variation is associated with the putative variable region segments of these isolates. Direct evidence is presented for **TCR** -like genes, which presumably are associated with T-cell function, at the earliest stages in the phylogenetic emergence of jawed vertebrates.

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L6 ANSWER 10 OF 13 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 94179857 MEDLINE
DOCUMENT NUMBER: 94179857 PubMed ID: 7510755
TITLE: A consensus primer to amplify both alpha and beta chains of the human T cell receptor.
AUTHOR: Moonka D; Loh E Y
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania Medical Center, Philadelphia.
CONTRACT NUMBER: AI33214 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1994 Feb 28) 169 (1) 41-51.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19960129
Entered Medline: 19940418

AB The use of reverse transcriptase in conjunction with the polymerase chain reaction (RT-**PCR**) has proven invaluable in the analysis of the **T cell receptor** (**TCR**) repertoire of different populations of T cells. However, the presence of a variable region in the **T cell receptor** has hindered the design of **primers** for the 5' end of the **TCR** cDNA. We describe the design and use of a **degenerate** consensus **primer** that allows amplification of both the alpha and **beta** chains of the human **TCR**. We have used this **primer** in the analysis of the **TCR** distribution of T cell clones, peripheral blood lymphocytes and lymphocytes residing in tissue. In addition, the **primer** has allowed the identification of an alternative splice site in the **beta** chain constant region which cannot translate into a functional constant region. We have found the **primer** to be easy to use, sensitive and specific.

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L6 ANSWER 11 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:270260 BIOSIS
DOCUMENT NUMBER: PREV199396000485
TITLE: Molecular cloning of major histocompatibility complex class I cDNAs from Atlantic salmon (Salmo salar.
AUTHOR(S): Grimholt, Unni Vvar Hordvik (1); Fosse, Viggo M.; Olsaker, Ingrid; Endresen, Curt; Lie, Oystein
CORPORATE SOURCE: (1) Dep. Animal Genetics, Norwegian College of Vet. Med., P.O. Box 8146 Dep., N-0033 Oslo 1 Norway
SOURCE: Immunogenetics, (1993) Vol. 37, No. 6, pp. 469-473. ISSN: 0093-7711.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The major histocompatibility complex (Mhc) has attracted much attention because of its immense polymorphism, its importance in transplantation, and its indisputable role in disease susceptibility in humans (Chen and Parham 1989; Hill et al. 1991) and in animals (Lie 1990). Previously, typical Mhc features reflected in allograft rejection and mixed leucocyte reactivity were the only indications that an Mhc also existed in teleost fish (Stet and Egberts 1991). The use of polymerase chain reaction (**PCR**) with **degenerate** oligonucleotides from conserved Mhc regions provided the first direct evidence for Mhc class I and class II genes in a fish, the teleost carp (Hashimoto et al. 1990). The primary aim of our study was to isolate and characterize expressed Mhc molecules in Atlantic salmon, and thereby provide data for further studies on evolutionary and disease aspects of the Mhc and its polymorphism. An atlantic salmon-specific Mhc probe from leucocyte RNA was generated by **PCR** based on **primers** from conserved regions of known Mhc genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik and co-workers (this issue). This salmon-specific probe was employed to screen a leucocyte lambda-gt10 cDNA library based on a few individuals, from which Mhc-positive cDNAs were derived. The cDNAs analyzed in this report were established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal **primers**, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using the UWGCG software (Devereux et al. 1984). The FASTA program (Pearson and Lipman 1988) was used to search the EMBL database. In accordance with the nomenclature proposed by Klein and co-workers (1990), we adopted the designation Mhc-Sasa, as proposed by Stet and Egberts (1991), for the two partial Atlantic salmon (Salmo salar) Mhc nucleotide sequences which we aligned to the EMBL database. One of these clones, p18, shared sequence similarity to Mhc class II molecules (Hordvik et al., this issue). The other clone, p23 (1.8 kilobase (kb)), showed sequence similarity to Mhc class I sequences with a non-translated tail of 1200 nucleotides (nt) and an open reading frame (orf) of 190 aminoacids (aa) starting in the middle of the alpha-2 domain (Fig. 1). The latter cDNA clone was used in a second screening of the cDNA library, which resulted in a potential full-length clone, Sasa p30 (2.8 kb), with an orf corresponding to 343 aa and a nontranslated tail of 1800 nt (Fig. 1). The domain boundaries of Sasa p30 were assigned by alignment with other Mhc class I molecule (Fig. 2). The aa sequence similarities between Sasa and Xenopua, and lizard, man, mouse, chicken, and carp are striking, and support the hypothesis that the isolated cDNA clones encode salmon Mhc class I molecules. Both and cysteines forming intrachain disulphide bonds within the alpha-2 and alpha-3 domains, and the potential glycosylation site at N-84 (numbering is based on the salmon sequence), are conserved. In the putative Sasa p30 transmembrane region there is a stretch of 21 hydrophobic residues flanked on both sides by hydrophilic segments, indicating a membrane anchored protein. Most of the residues assumed to be directly involved in the structure of the alpha-3 domain are conserved in the salmon sequence (C-198, F-203, Y-204, P-205, W-212, G-234, Y-254, C-256, and V-258; Williams et al. 1987). Nine residues pointing into the antigenic recognition site, and probably involved in recognizing constant features on processed antigens, are conserved in the alpha-1 and alpha-2 domains of humans and mice (Bjorkman et al. 1987). These residues are also conserved in the salmon sequence (L-5, Y-7, F-21, G-25, Y-57, T-140, K-143, Y-157, and Y-169). The signal peptide may be incomplete, as the cDNA clone started with a methionine residue. Both cDNA clones contained 17 repeated CA dinucleotides 110 nt after the first stop codon. This repeated sequence is polymorphic (data will be presented elsewhere), and can be used as an Mhc-linked marker. The two Sasa clones, p23 and p30, differed by 24 nt representing 14 aa residues (Fig. 1). Eleven of the variable aa positions

resided in the alpha-2 helical domain and only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human **T-cell receptor** interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only one substitution corresponded to a human, polymorphic, peptide-binding residue (res. 154). It is not possible to determine from our data whether the p23 and p30 cDNA clones are alleles or originate from different genes (isotypes). However, the clustering of replacement substitutions in the alpha-2 region, and the fact that the library from which the cDNA clones were selected was derived from several individuals, supports the hypothesis that the observed variation is attributable to allelism. An amino acid comparison between the salmon alpha domains and those of carp, chicken, HLA-A, H-2K, and lizard showed the significantly lowest similarity to carp (p lt 0.05). The low similarity between salmon and carp is also reflected in the phylogenetic tree (Fig. 3) based on the membrane-proximal aa sequences of Mhc class I (alpha-3) and class II (alpha-2 and **beta**-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is jointed to the H-2K/HLA-A node, but this is a doubtful result. Similarly, the evolutionary relationship between carp, Xenopus, and shark class I sequences are uncertain, and more Mhc class I sequences from lower vertebrates are needed to clarify the picture. All the class II sequences reside on the same branch. Shark class II is joined to a human class II alpha sequence, and the trout and salmon class II peptides are very similar and branched together with carp **beta**-2. Hashimoto and co-workers (1990) used **degenerate primers** directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast to the carp class II sequence, originates from a pseudogene and has thus acquired a considerable number of mutations. The carp class I sequence could also represent a nonclassical carp Mhc molecule. Both suggestions would explain why the carp class I sequence has the lowest overall alpha domain aa similarity (20%) to salmon. Further speculation on teleostean evolution must be deferred until further information is available on expressed carp Mhc class I sequences. A FASTA search with the p30 cDNA sequence identified 40 Mhc class I sequences as being most similar to the salmon sequence. These sequences included both nonclassical (mouse Q7(b), mouse T1a(c), and human HLA-G (HLA 6.0)) and classical Mhc class I genes. The question as to whether Atlantic salmon has both classical and nonclassical homologues, as seen in human and mouse, will be possible to answer when more Sasa loci have been identified. In conclusion, this study, together with the work done by Hordvik and co-workers (this issue), demonstrates the existence of expressed Mhc class I and class II molecules in Atlantic salmon. The clonal variation seen in these reports indicates allelic polymorphism as seen in other species, but the number of alleles and loci involved remains to be established. The teleost class II **beta**-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides is unclear. Further information on expressed carp class I sequences is needed to resolve this.

AB. . . only indications that an Mhc also existed in teleost fish (Stet and Egberts 1991). The use of polymerase chain reaction (**PCR**) with **degenerate** oligonucleotides from conserved Mhc regions provided the first direct evidence for Mhc class I and class II genes in a. . . and disease aspects of the Mhc and its polymorphism. An atlantic salmon-specific Mhc probe from leucocyte RNA was generated by **PCR** based on **primers** from conserved regions of known Mhc genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik. . . established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal **primers**, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using. . . only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human **T-cell receptor** interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only. . . phylogenetic tree (Fig. 3) based on the membrane-proximal aa sequences of Mhc class I (alpha-3) and class II (alpha-2 and **beta**-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is jointed. . . class II alpha sequence, and the trout and salmon class II peptides are very similar and branched together with carp **beta**-2. Hashimoto and co-workers (1990) used **degenerate primers** directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast. . . seen in other species, but the number of alleles and loci involved remains to be established. The teleost class II **beta**-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides. . .

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:606319 CAPLUS
DOCUMENT NUMBER: 117:206319
TITLE: Identification of cell subpopulations using modified PCR to amplify DNA encoding proteins with constant and variable regions
INVENTOR(S): Danska, Jayne S.; Fathman, Garrison C.
PATENT ASSIGNEE(S): Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9119816	A1	19911226	WO 1991-US4317	19910617
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2086015	AA	19911221	CA 1991-2086015	19910617

PRIORITY APPLN. INFO.: US 1990-541123 19900620

AB A method for amplifying DNA encoding a protein having a const. and variable region by a polymerase chain reaction (**PCR**) modification is described. The method employs 2 **primers**, one of which is complementary to a const. region. The other is a **degenerate primer** complementary to a portion of the DNA encoding a consensus sequence. The amplified DNA can be cloned and sequenced, so that the cells expressing the protein can be identified. The resulting information can be used to design therapies for autoimmune diseases, lymphomas, and leukemias (no data). This procedure was applied

to amplification, cloning, and sequencing of mouse **T-cell receptor** .alpha. and .**beta**. cDNA fragments comprising V and J regions.

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L6 ANSWER 13 OF 13 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 91184261 MEDLINE
DOCUMENT NUMBER: 91184261 PubMed ID: 2009906
TITLE: Conserved nucleotide sequences at the 5' end of T cell receptor variable genes facilitate polymerase chain reaction amplification.
AUTHOR: Broeren C P; Verjans G M; Van Eden W; Kusters J G; Lenstra J A; Logtenberg T
CORPORATE SOURCE: Institute of Infectious Diseases and Immunology, School of Veterinary Medicine, University of Utrecht, The Netherlands.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Mar) 21 (3) 569-75. Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19910526
Entered Medline: 19910503

AB Alignment of all available nucleotide sequences of mouse and rat alpha/**beta T cell receptor** (**TcR**) variable (V) regions revealed the presence of relatively conserved sequences at the 5' end of the V gene segments. Based on these conserved sequences, **degenerate primers** were developed for use in the polymerase chain reaction (**PCR**). The **degenerate primers** developed on the basis of the conserved sequences at the 5' end of rat and mouse V gene segments are expected to enable the amplification of all mouse and rat **TcR** alpha/**beta** chain V regions. To test their applicability, the **primers** were used for the amplification of the V region of the **TcR** alpha/**beta** expressed by rat T cell lines. After amplification, the **TcR** V regions expressed were cloned and sequenced. The Z1a T cell line was shown to use the same **TcR** V gene segments (V alpha 2 and V **beta** 8.2), as most other experimental allergic encephalomyelitis associated T cell lines, but had different D and J segments. In spite of these differences at the nucleotide level, a remarkable conservation of the amino acid sequence at the V **beta** D **beta** J **beta** junction was found. Alignment of a large number of human V alpha and V **beta** gene segments revealed the presence of similarly conserved sequences. **Degenerate primers** based on these conserved sequences enabled the amplification of **TcR** V regions of human T cell lines.

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```
=> s dis his
L7            0 DIS HIS

=> dis his

     (FILE 'HOME' ENTERED AT 17:22:59 ON 29 AUG 2001)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:23:11 ON 29 AUG 2001
L1          589 S (PCR OR RTPCR) (P) (TCR OR (T CELL RECEPTOR?)) (P) (BETA) (P)
L2          495 S L1 AND PY < 1998
L3           27 S L2 AND DEGENERATE
L4            9 DUP REM L3 (18 DUPLICATES REMOVED)
L5           34 S L1 AND DEGENERATE
L6           13 DUP REM L5 (21 DUPLICATES REMOVED)
L7            0 S DIS HIS

=> s l1 and NZ?
L8            0 L1 AND NZ?

=> s NZ? and TCR and PCR and primer? and oligo?
L9            0 NZ? AND TCR AND PCR AND PRIMER? AND OLIGO?

=> s M11? and TCR and PCR and primer? and oligo?
L10           0 M11? AND TCR AND PCR AND PRIMER? AND OLIGO?

=> s MJ? and TCR and PCR and primer? and oligo?
L11           0 MJ? AND TCR AND PCR AND PRIMER? AND OLIGO?
```

```
=> s MJ? and (T cell receptor?) and PCR
   3 FILES SEARCHED...
L12          1 MJ? AND (T CELL RECEPTOR?) AND PCR

=> dis l12 ibib abs kwic

L12  ANSWER 1 OF 1  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   2000209063  EMBASE
TITLE:              A PCR-SSP method to specifically select
                    HLA-A*0201 individuals for immunotherapeutic studies.
AUTHOR:             Gatz S.A.; Pohla H.; Schendel D.J.
CORPORATE SOURCE:   D.J. Schendel, Institut fur Molekulare Immunologie, GSF
                    Forsch. Umwelt und Gesundheit, Marchioninistrasse 25, 81377
                    Munich, Germany. schendel@gsf.de
SOURCE:             Tissue Antigens, (2000) 55/6 (532-547).
                    Refs: 51
                    ISSN: 0001-2815  CODEN: TSANA2
COUNTRY:            Denmark
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       026     Immunology, Serology and Transplantation
                    029     Clinical Biochemistry
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   HLA-A*0201 is an important restriction element for peptide presentation to
     T cells in disease and cancer. Mutation studies and analyses using
     cytotoxic T lymphocytes have shown the functional relevance of
     subtype-specific differences in HLA-A2 molecules for peptide binding and
     T-cell receptor recognition. Therefore, many
     immunotherapeutic studies need to accurately select HLA-A*0201-positive
     individuals. We designed an easy, robust approach based on the polymerase
     chain reaction using sequence-specific primers (PCR-SSP) to
     specifically distinguish A*0201-positive individuals from other HLA-A2
     subtypes described to date. The first step includes reactions that give
     information whether the sample donor is HLA-A2 and, if so, whether the
     individual is homozygous or heterozygous for HLA-A2. Further, it is
     determined whether the sample has an HLA-A*0209 or an HLA-A*0201 sequence
     at the corresponding position in exon 4. Samples that may contain an
     HLA-A*0201 allele according to the results of this first step are subtyped
     in a second step nested PCR. Here the strategy is focussed on
     the discrimination of HLA-A*0201 from the other subtypes by considering
     divergent nucleotide positions in two ways. One SSP combination amplifies
     the HLA-A*0201 sequence while a corresponding SSP combination specifically
     amplifies the subtype or group of subtypes differing from HLA-A*0201 at
     this position. Thus, at relevant polymorphic nucleotide positions the
     HLA-A*0201 sequence is both directly and indirectly confirmed. This
     strategy strongly enhances the reliability of the subtyping and allows
     better verification of HLA-A*0201-positive patient selection for clinical
     studies.
TI   A PCR-SSP method to specifically select HLA-A*0201 individuals
     for immunotherapeutic studies.
AB   . . . analyses using cytotoxic T lymphocytes have shown the functional
     relevance of subtype-specific differences in HLA-A2 molecules for peptide
     binding and T-cell receptor recognition.
     Therefore, many immunotherapeutic studies need to accurately select
     HLA-A*0201-positive individuals. We designed an easy, robust approach
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     PCR-SSP) to specifically distinguish A*0201-positive individuals
     from other HLA-A2 subtypes described to date. The first step includes
     reactions that give information. . . may contain an HLA-A*0201 allele
     according to the results of this first step are subtyped in a second step
     nested PCR. Here the strategy is focussed on the discrimination
     of HLA-A*0201 from the other subtypes by considering divergent nucleotide
     positions in. . .
CO   (2) Becton Dickinson (United States) ; (3) MJ Research (United
     States)


=>  dis his

     (FILE 'HOME' ENTERED AT 17:22:59 ON 29 AUG 2001)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:23:11 ON 29 AUG 2001
L1           589 S (PCR OR RTPCR) (P) (TCR OR (T CELL RECEPTOR?)) (P) (BETA) (P)
L2           495 S L1 AND PY < 1998
L3            27 S L2 AND DEGENERATE
L4             9 DUP REM L3 (18 DUPLICATES REMOVED)
L5            34 S L1 AND DEGENERATE
L6            13 DUP REM L5 (21 DUPLICATES REMOVED)
L7             0 S DIS HIS
L8             0 S L1 AND NZ?
L9             0 S NZ? AND TCR AND PCR AND PRIMER? AND OLIGO?
L10            0 S M11? AND TCR AND PCR AND PRIMER? AND OLIGO?
L11            0 S MJ? AND TCR AND PCR AND PRIMER? AND OLIGO?
L12            1 S MJ? AND (T CELL RECEPTOR?) AND PCR

=> s l1 and (degenerate or consensus)
L13           60 L1 AND (DEGENERATE OR CONSENSUS)

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14           23 DUP REM L13 (37 DUPLICATES REMOVED)

=> dis l14 1-23 ibib abs kwic

L14  ANSWER 1 OF 23     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2001099135     MEDLINE
DOCUMENT NUMBER:    20565479   PubMed ID: 11113282
TITLE:              T-cell antigen receptors in Atlantic cod (Gadus morhua l.):
                    structure, organisation and expression of TCR alpha and
                    beta genes.
AUTHOR:             Wermenstam N E; Pilstrom L
CORPORATE SOURCE:   Immunology Programme, Department of Cell and Molecular
                    Biology, BMC, Uppsala University, Box 596, S-751 24,
                    Uppsala, Sweden.
SOURCE:             DEVELOPMENTAL AND COMPARATIVE IMMUNOLOGY, (2001 Mar) 25 (2)
                    117-35.
                    Journal code: E3M. ISSN: 0145-305X.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
```

OTHER SOURCE: GENBANK-AJ133844; GENBANK-AJ133845; GENBANK-AJ133846; GENBANK-AJ133847; GENBANK-AJ133848; GENBANK-AJ133849; GENBANK-AJ133850; GENBANK-AJ133851
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and constant region segments for **PCR**, we were able to isolate putative TCRalpha and **beta** chain full length cDNAs in Atlantic cod. The Valpha and Vbeta domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The Jalpha and Jbeta region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and immunoglobulin light chain J regions. Similar to other vertebrates, the Atlantic cod Calpha and Cbeta sequences exhibit distinct immunoglobulin, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod Cbeta sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerisation and cell surface expression are observed. Four different cod Cbeta sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of Cbeta. Based on Southern blot analyses, the TCRalpha and **beta** gene loci appear to be arranged in translocon organisation (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the TCRalpha and **beta** chains in thymus, spleen and head kidney, expression of the TCRbeta chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

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L14 ANSWER 2 OF 23 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:315041 BIOSIS
DOCUMENT NUMBER: PREV200100315041
TITLE: Rapid cloning of complete T cell receptor variable regions for immunotherapy.
AUTHOR(S): Reddy, Sunil A. (1); Levy, Ronald (1)
CORPORATE SOURCE: (1) Oncology, Stanford University Medical Center, Stanford, CA USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 830a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Several strategies exist to clone **T cell receptor** (**TCR**) genes. Many methodologies involve the use of **TCR** gene family specific **primers** but do not necessarily provide an easy way to obtain complete variable region sequences. Complete variable region genes are important for applications such as **TCR** idiotype(**TCR-Id**) vaccine therapy, study of **TCR** polymorphisms and the study of **TCR** repertoire in health and disease at the sequence level. One strategy that avoids using multiple family specific **primers** (>20 families of alpha and **beta** chains) is RACE (Rapid amplification of cDNA ends). This strategy works well but is marred by frequent truncated clones and long **PCR** procedure involving two rounds of Polymerase Chain Reaction (**PCR**) and multiple gel extractions. The lengthy procedure opens one up to contamination making analysis of clonality very difficult. We have used a modification of RACE, developed by Chenchik and colleagues (CLONOTECHniques X(1):5-8), known as Smart **PCR** (Switching Mechanism At 5' end of RNA Transcript). Like traditional RACE, this process enables formation of a **consensus primer** at the 5' end of mRNA avoiding the need for 5' **TCR** family specific **primers**. This process also enriches for complete transcripts by taking advantage of physiologic addition of C's by Reverse Transcriptase to completed cDNA. Specificity is then obtained by using **TCR** constant region **primers** at the 3' end for **PCR**. In addition, the use of touchdown **PCR** (NAR. 19:4008) enables linear amplification of the cDNA of interest prior to exponential **PCR**. We have investigated this on a series of benign and malignant T cell cases. Control samples include spongiotic dermatitis, drug hypersensitivity, peripheral blood lymphocytes, and reactive tonsils. Tumor samples include Mycosis Fungoides(MF) lymph nodes, skin plaque and skin tumor samples. MF is known to contain as few as 10% malignant cells in tumor lesions. Monoclonal bands can be obtained from tumor samples with as few as 15 cycles of **PCR**. We are even able to obtain bands on small MF skin samples that were refractory to traditional RACE amplification. After cloning of the **PCR** product, sequencing shows that almost all clones (>95%) contain complete alpha and **beta TCR** sequences. This is in comparison to a 50% complete transcript rate with traditional RACE. We are also able to identify the malignant clone using this methodology. In our hands, this method is now validated for use in the detailed analysis of clonal populations in reactive skin diseases and malignant lesions. Finally, we would like to apply this cloning strategy for use in **TCR-Id** vaccines for treatment of T cell lymphomas.

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L14 ANSWER 3 OF 23 MEDLINE
ACCESSION NUMBER: 2000411646 MEDLINE
DOCUMENT NUMBER: 20394656 PubMed ID: 10938743
TITLE: Immunopurification of T-cells from sea bass Dicentrarchus labrax (L.).
AUTHOR: Scapigliati G; Romano N; Abelli L; Meloni S; Ficca A G; Buonocore F; Bird S; Secombes C J
CORPORATE SOURCE: Dipartimento di Scienze Ambientali, Universita della Tuscia, Viterbo, Italy.. scapigg@unitus.it
SOURCE: FISH & SHELLFISH IMMUNOLOGY, (2000 May) 10 (4) 329-41. Journal code: DR8; 9505220. ISSN: 1050-4648.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829

AB The monoclonal antibody DLT15, specific for thymocytes and peripheral T-cells of the teleost fish Dicentrarchus labrax (sea bass), was used to purify immunoreactive cells from blood and gut-associated lymphoid tissue. The purification was performed by immuno-magnetic sorting of leucocyte fractions enriched by Percoll density gradient centrifugation, and the purity of the isolated cells was estimated by cytofluorimetric analysis. Following a single step, the percentage of DLT15-purified cells was 88 +/- 10% for gut-associated lymphoid tissue and 79 +/- 18% for blood leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-**PCR** experiments using as **primers** **degenerate** oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout **TcR** **beta** chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV **beta** 3. By 3'-RACE the cDNA was elongated to obtain the **TcR** constant region, with high similarity to other fish **TcR** sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.

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L14 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:853499 CAPLUS
TITLE: T-cell antigen receptors in Atlantic cod (Gadus morhua L.): structure, organisation and expression of TCR .alpha. and .beta. genes
AUTHOR(S): Wermenstam, N. E.; Pilstrom, L.
CORPORATE SOURCE: BMC, Department of Cell and Molecular Biology, Immunology Programme, Uppsala University, Uppsala, S-751 24, Swed.
SOURCE: Dev. Comp. Immunol. (2000), 25(2), 117-135
CODEN: DCIMDQ; ISSN: 0145-305X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By using short **degenerate** **primers** complementing conserved T-cell antigen receptor (**TCR**) variable and const. region segments for **PCR**, we were able to isolate putative **TCR**.alpha. and .**beta**. chain full length cDNAs in Atlantic cod. The V.alpha. and V.**beta**. domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.**beta**. region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C. **beta**. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.**beta**. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface

expression are obsd. Four different cod C.**beta**. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.**beta**.. Based on Southern blot analyses, the **TCR**.alpha. and .**beta**. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the **TCR** .alpha. and .**beta**. chains in thymus, spleen and head kidney, expression of the **TCR**.**beta**. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

REFERENCE COUNT: 57
REFERENCE(S): (2) Alcover, A; J Biol Chem 1990, V265, P4131 CAPLUS
(3) Arnaud, J; Int Immunol 1997, V9, P615 CAPLUS
(5) Backstrom, B; Science 1998, V281, P835 CAPLUS
(6) Bengten, E; Dev Comp Immunol 1994, V18, P109 CAPLUS
(7) Bengten, E; Eur J Immunol 1991, V21, P3027 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and const. region segments for **PCR**, we were able to isolate putative **TCR**.alpha. and .**beta**. chain full length cDNAs in Atlantic cod. The V.alpha. and V.**beta**. domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.**beta**. region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.**beta**. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.**beta**. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are obsd. Four different cod C.**beta**. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.**beta**.. Based on Southern blot analyses, the **TCR**.alpha. and .**beta**. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the **TCR** .alpha. and .**beta**. chains in thymus, spleen and head kidney, expression of the **TCR**.**beta**. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

L14 ANSWER 5 OF 23 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999290761 MEDLINE
DOCUMENT NUMBER: 99290761 PubMed ID: 10361104
TITLE: Ig heavy chain gene rearrangements in T-cell acute lymphoblastic leukemia exhibit predominant DH6-19 and DH7-27 gene usage, can result in complete V-D-J rearrangements, and are rare in T-cell receptor alpha beta lineage.
AUTHOR: Szczepanski T; Pongers-Willemse M J; Langerak A W; Harts W A; Wijkhuijs A J; van Wering E R; van Dongen J J
CORPORATE SOURCE: Department of Immunology, University Hospital Rotterdam/Erasmus University Rotterdam, Rotterdam, The Netherlands.
SOURCE: BLOOD, (1999 Jun 15) 93 (12) 4079-85.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714
Entered Medline: 19990701

AB Rearranged IGH genes were detected by Southern blotting in 22% of 118 cases of T-cell acute lymphoblastic leukemia (ALL) and involved monoallelic and biallelic rearrangements in 69% (18/26) and 31% (8/26) of these cases, respectively. IGH gene rearrangements were found in 19% (13/69) of CD3(-) T-ALL and in 50% of TCRgammadelta+ T-ALL (12/24), whereas only a single TCRalpha **beta**+ T-ALL (1/25) displayed a monoallelic IGH gene rearrangement. The association with the **T-cell receptor** (**TCR**) phenotype was further supported by the striking relationship between IGH and **TCR** delta (TCRD) gene rearrangements, ie, 32% of T-ALL (23/72) with monoallelic or biallelic TCRD gene rearrangements had IGH gene rearrangements, whereas only 1 of 26 T-ALL with biallelic TCRD gene deletions contained a monoallelic IGH gene rearrangement. Heteroduplex polymerase chain reaction (**PCR**) analysis with VH and DH family-specific **primers** in combination with a JH **consensus primer** showed a total of 39 clonal products, representing 7 (18%) VH-(DH-)JH joinings and 32 (82%) DH-JH rearrangements. Whereas the usage of VH gene segments was seemingly random, preferential usage of DH6-19 (45%) and DH7-27 (21%) gene segments was observed. Although the JH4 and JH6 gene segments were used most frequently (33% and 21%, respectively), a significant proportion of joinings (28%) used the most upstream JH1 and JH2 gene segments, which are rarely used in precursor-B-ALL and normal B cells (1% to 4%). In conclusion, the high frequency of incomplete DH-JH rearrangements, the frequent usage of the more downstream DH6-19 and DH7-27 gene segments, and the most upstream JH1 and JH2 gene segments suggests a predominance of immature IGH rearrangements in immature (non-TCRalpha **beta**+) T-ALL as a result of continuing V(D)J recombinase activity. More mature alpha **beta**-lineage T-ALL with biallelic TCRD gene deletions apparently have switched off their recombination machinery and are less prone to cross-lineage IGH gene rearrangements. The combined results indicate that IGH gene rearrangements in T-ALL are postoncogenic processes, which are absent in T-ALL with deleted TCRD genes and completed **TCR** alpha (TCRA) gene rearrangements.

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L14 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
ACCESSION NUMBER: 1999:605448 CAPLUS
DOCUMENT NUMBER: 132:149888
TITLE: Rearranged T lymphocyte antigen receptor genes as markers of malignant T cells
AUTHOR(S): Dreitz, M. J.; Ogilvie, G.; Kee Sim, G.
CORPORATE SOURCE: HESKA Corporation, Ft. Collins, CO, USA
SOURCE: Vet. Immunol. Immunopathol. (1999), 69(2-4), 113-119
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have recently cloned a no. of canine **T cell receptor** (**TCR**) V.**beta**. genes using **degenerate** oligonucleotides. From the DNA sequences of the resulting clones and the canine V.**beta**. gene sequences in the literature, seven distinct canine **TCR** V.**beta**. genes were identified. V.**beta**. specific **PCR primers** were designed for each of the seven **TCR** V.**beta**. genes such that under defined conditions, each **primer** could only amplify a specific **TCR** V.**beta**. gene in conjunction with the same 3' const. region (C.**beta**.) **primer**. By performing RT-**PCR** on RNA derived from a source contg. T lymphocytes, the presence and expansion of T cells expressing a particular V.**beta**. gene could be detected. Moreover, the clonality or diversity of a T cell population under anal. could be easily detd. by the VDJ junctional sequence of the amplified V.**beta**. **PCR** product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.
REFERENCE COUNT: 10
REFERENCE(S): (2) Davis, M; Nature 1988, V334, P395 CAPLUS
(3) Hood, L; Cell 1985, V40, P225 CAPLUS
(4) Ito, K; Immunogenetics 1993, V38, P60 CAPLUS
(5) Malissen, M; Cell 1984, V37, P1101 CAPLUS
(6) Patten, P; Nature 1984, V312, P40 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB We have recently cloned a no. of canine **T cell receptor** (**TCR**) V.**beta**. genes using **degenerate** oligonucleotides. From the DNA sequences of the resulting clones and the canine V.**beta**. gene sequences in the literature, seven distinct canine **TCR** V.**beta**. genes were identified. V.**beta**. specific **PCR primers** were designed for each of the seven **TCR** V.**beta**. genes such that under defined conditions, each **primer** could only amplify a specific **TCR** V.**beta**. gene in conjunction with the same 3' const. region (C.**beta**.) **primer**. By performing RT-**PCR** on RNA derived from a source contg. T lymphocytes, the presence and expansion of T cells expressing a particular V.**beta**. gene could be detected. Moreover, the clonality or diversity of a T cell population under anal. could be easily detd. by the VDJ junctional sequence of the amplified V.**beta**. **PCR** product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.

L14 ANSWER 7 OF 23 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999052788 MEDLINE
DOCUMENT NUMBER: 99052788 PubMed ID: 9836068
TITLE: Improved polymerase chain reaction detection of clonally rearranged T-cell receptor beta chain genes.
AUTHOR: Zemlin M; Hummel M; Anagnostopoulos I; Stein H
CORPORATE SOURCE: Konsultations- und Referenzzentrum fur Lymphknoten- und Hamatopathologie, Klinikum Benjamin Franklin, Free University Berlin, Germany.
SOURCE: DIAGNOSTIC MOLECULAR PATHOLOGY, (1998 Jun) 7 (3) 138-45.
Journal code: BY3; 9204924. ISSN: 1052-9551.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990204
AB A new method for the detection of all known possible rearrangements at the variable (V), diversity (D), and joining (J) segments of the **T-cell receptor beta** chain (**TcR beta**) gene in tissue DNA extracts is described that involves two polymerase chain reactions (**PCRs**). The first **PCR** round (screening **PCR**) allowed the identification of the J **beta** segment involved in a clonal rearrangement. A J **beta-primer** was used for the second **PCR** (J **beta** -specific **PCR**), recognizing the J **beta** segment identified in the screening **PCR** in combination with a **consensus** V **beta primer**. This **PCR** generated prominent and short amplificates suitable for direct sequence analysis because of their low background. Using this approach, clonal **TcR beta** gene rearrangements were able to be demonstrated in all T-cell lines (n = 7) and in all peripheral T-cell lymphomas (n = 33) analyzed. No clonal **TcR beta** gene rearrangements were found in any of the normal tissues studied nor in any B-cell non-Hodgkin lymphomas. This method is applicable to DNA from fresh frozen tissues, and, after the **TcR beta** rearrangement of a patient's malignant T-cell clone has been identified by the screening **PCR**, DNA can also be detected in follow-up formalin-fixed

paraffin-embedded samples by the J **beta**-specific **PCR** with high sensitivity and specificity.

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L14 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:733370 CAPLUS
DOCUMENT NUMBER: 128:44336
TITLE: Human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer
AUTHOR(S): Moonka, Dilip K.; Loh, Elwyn Y.
CORPORATE SOURCE: Department Medicine, Division Gastrointestinal Diseases, University Pennsylvania Medical Center Cancer Center, Philadelphia, PA, USA
SOURCE: Antigen T Cell Recept. (1997), 238-265. Editor(s): Oksenberg, Jorge R. Landes: Austin, Tex. CODEN: 65HEAM
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The detn. of the variable and joining sequences of **T cell receptors** in different human T cell populations is of interest in many biol. contexts. The use of reverse transcriptase to synthesize cDNA from mRNA followed by **PCR** has greatly facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific **primers** for the 5' end. This work describes a **degenerate, consensus primer** that binds to a relatively conserved area of the human .alpha. and .**beta**. **TCR** variable region.

TI Human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer

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IT Genes (animal)
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Tcr; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT RT-**PCR** (reverse transcription-polymerase chain reaction)
(human **T cell receptor** alpha and **beta** chain cDNA amplification with a **consensus primer**)

IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT cDNA
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT TCR (T cell receptors)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha. and .beta. chains; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 138262-64-3
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer ANB; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-45-0
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer ANB.alpha.3; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-46-1
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer CA1; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-47-2
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer CA2; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-48-3
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(primer CA3; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-49-4
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer CB1; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-50-7
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer CB2; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

IT 199878-51-8
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer CB3; human T cell receptor alpha and beta chain cDNA amplification with a **consensus** primer)

L14 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:252051 CAPLUS
DOCUMENT NUMBER: 126:259755
TITLE: Additional TCRV.beta. primers and minor method modifications improve detection of clonal T-cell populations by RT-PCR
AUTHOR(S): Lynas, C.; Howe, D.
CORPORATE SOURCE: Dep. Haematology, Derriford Hospital, Plymouth, PL6 8DH, UK
SOURCE: Mol. Pathol. (1997), 50(1), 53-55
CODEN: MOPAF6
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The TCRV.beta. RT-PCR method for detection of clonal populations of T cells which we described previously could not detect clones that used certain variable (V) .beta. region families. V.beta. 2, 4, 8.3, and 18 had insufficient homol. with the original **consensus** V region primer. Two new primers have been designed which work well and are able to amplify from V.beta. families previously undetectable by this RT-PCR. In addn., minor alterations to the cDNA synthesis and gel anal. of the PCR products make the results even easier to interpret. All the Diversity/Joining (D/J) region primer combinations except for D2/J2 have been omitted, and terminating the reverse transcription by heating prior to PCR greatly improves amplification with these primers. Use of 8% and/or 10% polyacrylamide gels increases clarity. Inclusion of the modifications described will reduce false reporting of patients as having a polyclonal T-cell population.

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IT **TCR (T-cell receptors)**
RL: ARU (Analytical role, unclassified); BOC (Biological occurrence); PRP (Properties); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(**.beta.**-chain, V region; addnl. TCRV.**beta.** **primers** and minor method modifications improve detection of clonal T-cell populations by RT-**PCR**)

L14 ANSWER 10 OF 23 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97205328 MEDLINE
DOCUMENT NUMBER: 97205328 PubMed ID: 9052832
TITLE: alpha, beta, gamma, and delta T cell antigen receptor genes arose early in vertebrate phylogeny.
AUTHOR: Rast J P; Anderson M K; Strong S J; Luer C; Litman R T; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: R37 AI23338 (NIAID)
SOURCE: IMMUNITY, (1997 Jan) 6 (1) 1-11.
Journal code: CCF; 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U75747; GENBANK-U75748; GENBANK-U75749; GENBANK-U75750; GENBANK-U75751; GENBANK-U75752; GENBANK-U75753; GENBANK-U75754; GENBANK-U75755; GENBANK-U75756; GENBANK-U75757; GENBANK-U75758; GENBANK-U75759; GENBANK-U75760; GENBANK-U75761; GENBANK-U75762; GENBANK-U75763; GENBANK-U75764; GENBANK-U75765; GENBANK-U75766; GENBANK-U75767; GENBANK-U75768; GENBANK-U75769; GENBANK-U75770; GENBANK-U75771; GENBANK-U75772; GENBANK-U75773; GENBANK-U75774; GENBANK-U75775; GENBANK-U75776; +
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970331

AB A series of products were amplified using a **PCR** strategy based on short minimally **degenerate primers** and R. eglanteria (clearnose skate) spleen cDNA as template. These products were used as probes to select corresponding cDNAs from a spleen cDNA library. The cDNA sequences exhibit significant identity with prototypic (alpha, **beta**, gamma, and delta T cell antigen receptor (**TCR**) genes. Characterization of cDNAs reveals extensive variable region diversity, putative diversity segments, and varying degrees of junctional diversification. This demonstrates expression of both alpha/**beta** and gamma/delta **TCR** genes at an early level of vertebrate phylogeny and indicates that the three major known classes of rearranging

antigen receptors were present in the common ancestor of the present-day jawed vertebrates.

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L14 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:736326 CAPLUS
DOCUMENT NUMBER: 126:15272
TITLE: Detection of clonal rearrangement of the T-cell receptor gamma gene by polymerase chain reaction and single-strand conformation polymorphism (PCR-SSCP)
AUTHOR(S): Kaul, Karen; Petrick, Marcia; Herz, Barbara; Cheng, Ta-Chih Philip
CORPORATE SOURCE: Medical School, Northwestern University, Evanston, IL, 60201, USA
SOURCE: Mol. Diagn. (1996), 1(2), 131-137
CODEN: MDIAFU; ISSN: 1084-8592
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diagnosis of T-lymphoid neoplasms frequently requires mol. studies of **T-cell receptor** (**TCR**) gene rearrangements. The Southern blot technique traditionally used for these analyses lacks the sensitivity and speed necessary for the routine clin. lab. The authors have developed a method using polymerase chain reaction (**PCR**) amplification with single-strand conformation polymorphism (SSCP) anal. that is rapid, sensitive, and semiautomated. Methods and Results: Polymerase chain reaction of the **TCR** gamma gene is done with **consensus primers** to the V and J regions. Amplicons thus include the N region, which serves as a marker of a clonal T-cell population. Clonal populations having identical N-region sequences are identified by SSCP anal., using a semiautomated electrophoresis system with silver staining for gel visualization. A series of 46 DNA samples from normal controls and various hematopoietic malignancies was comparatively analyzed by both Southern blot of the **TCR** **beta** locus and **PCR**-SSCP of the **TCR** gamma gene. The **PCR**-SSCP technique was rapid and reproducible, and detected clonal T-cell populations constituting 1% of the cell sample: The **PCR**-SSCP technique detected clones in eight cases that were neg. by Southern blot. Conclusions: **PCR**-SSCP anal. of the **TCR** gamma gene is a rapid and sensitive method for the detection of clonal T-cell populations.

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L14 ANSWER 12 OF 23 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96194879 MEDLINE
DOCUMENT NUMBER: 96194879 PubMed ID: 8625946
TITLE: TCR beta PCR from crude preparations for restriction digest or sequencing.
AUTHOR: Clark L S; Nicklas J A
CORPORATE SOURCE: Vermont Cancer Center Genetics Laboratory, University of Vermont, Burlington, 05401, USA.
CONTRACT NUMBER: CA30688 (NCI)
SOURCE: ENVIRONMENTAL AND MOLECULAR MUTAGENESIS, (1996) 27 (1) 34-8.
Journal code: EMM; 8800109. ISSN: 0893-6692.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19960708
Entered Medline: 19960625

AB T cell specificity is determined by the combinatorial association of specific variable (V), diversity (D), and junctional (J) regions. Clones of T cells (clonality) can occur, in the blood or in tissue, after proliferation of activated T cells. Determining clonality in mutation assays is necessary to distinguish between mutants and mutational events. We have developed a novel approach to determine clonality among T cell isolates, using restriction digests of **PCR**-amplified cDNA of the **T cell receptor beta** gene. The **T cell receptor beta** gene was **PCR**-amplified by use of a **consensus primer**, beginning from a cell pellet of 2,000-5,000 cells or from extracted RNA. This **TCR** (**T cell receptor**) **beta** chain **PCR** product can also be directly sequenced, allowing simple and easy identification of Vbeta and CDR3 sequence from a small number of cells. The utility of this method is demonstrated by **PCR**, restriction digest, and sequencing of the **TCR** **beta** cDNA from eight T cell clones isolated from 2 individuals. A

clone of three identical isolates (one 3-mer) and a clone of two identical isolates (one 2-mer) were determined from restriction digests using two different enzymes. This new method is an easier and more rapid way of determining clonality than traditional methods, e.g., Southern blotting.

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L14 ANSWER 13 OF 23 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 96068761 MEDLINE
DOCUMENT NUMBER: 96068761 PubMed ID: 7579363
TITLE: Analysis of rearranged T-cell receptor beta-chain genes by polymerase chain reaction (PCR) DNA sequencing and automated high resolution PCR fragment analysis.
AUTHOR: Kneba M; Bolz I; Linke B; Hiddemann W
CORPORATE SOURCE: Department of Internal Medicine, Georg-August University, Goettingen, Germany.
SOURCE: BLOOD, (1995 Nov 15) 86 (10) 3930-7.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951219

AB Polymerase chain reaction (**PCR**)-directed amplification and sequencing of rearranged immune genes for identification of clone-specific markers are increasingly being used in acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma (NHL) patients instead of the time consuming and labor intensive Southern analysis. In previous reports, no single common V **beta** and J **beta** sequence had been identified that allowed reliable amplification of the majority of rearranged T-cell antigen receptor (**TCR**)-**beta** V-D-J junctions at the DNA level because of the relatively large number of possible **TCR**-**beta** variable (V **beta**) and joining (J **beta**) gene segments involved in the rearrangement processes. In the present study we designed highly **degenerate PCR primers** directed against conserved sequences of the J **beta** genes. IN combination with a previously published **consensus** V **beta primer**, these J **beta primers** specifically amplify **TCR**- **beta** V-N(D)N-J junctions from genomic DNA. Using this approach we studied DNA extracted from biopsy material of nine patients with T-cell lymphoproliferative disorders, one c-ALL patient, and five patients with nonmalignant diseases. T-cell lines Molt 3, Jurkat, and HM 2 served as monoclonal controls. Individual **PCR** products were sequenced after cloning. The nucleotide sequences of 96 randomly chosen recombinant vectors were determined. In the polyclonal controls all analyzed clones differed in their **TCR**-**beta** V-N(D)N-J junctions. In the T-cell lines, in all of the T-cell malignancies, and in the c-ALL, monoclonal **PCR** products could be identified by demonstration of clonally restricted V-N(D)N-J junctions. The **PCR** results were confirmed by automated fluorescence quantification and size determination of **PCR** products after separation in a high-resolution polyacrylamide gel. The procedure allows rapid and specific characterization of clonal **TCR**-**beta** rearrangements from genomic DNA and will significantly simplify current experimental approaches to identify and to quantitate malignant T cells during initial staging and follow-up of T-lineage NHL and ALL patients.

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L14 ANSWER 14 OF 23 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 96153658 MEDLINE
DOCUMENT NUMBER: 96153658 PubMed ID: 8575839
TITLE: V gamma (I) expression in human intestinal lymphocytes is restricted.
AUTHOR: Landau S B; Aziz W I; Woodcock-Mitchell J; Melamede R
CORPORATE SOURCE: Department of Medicine, University of Vermont, Burlington,

USA.
SOURCE: IMMUNOLOGICAL INVESTIGATIONS, (1995 Nov) 24 (6) 947-55.
Journal code: GI5; 8504629. ISSN: 0882-0139.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960321
Last Updated on STN: 19960321
Entered Medline: 19960311

AB The majority of human intestinal intraepithelial lymphocytes (HIELS) express CD8+, and the **T cell Receptor** (**TCR**) alpha **beta**. A minority of HIELS utilize **TCR** gamma delta chains. V delta 1 is established as the **TCR**-delta expressed by most **TCR** gamma delta HIELS. Since V delta 1 is the dominant intestinal **TCR** and V gamma (I) family is preferentially used in forming a heterodimer, this study was conducted to characterize individual V gamma (I) utilization in HIELS. Intestinal lymphocytes were isolated from four samples of colonic epithelium obtained from patients undergoing colon resection or endoscopy. RNA was isolated and cDNA synthesized. **PCR** amplification was performed with **consensus** J gamma and V gamma **primers** in these regions. **PCR** products were cloned and sequenced. All samples had V gamma 4 transcripts, a majority V gamma 3 whereas V gamma 2 and V gamma 8 were less frequent. No V gamma 2 transcripts had any predicted **TCR** protein products. Similarly, very few potentially productive V gamma 3 transcripts were found. In contrast, almost all V gamma 4 transcripts were found to be in-frame and the only V gamma 8 transcript was in-frame. The CDR3 region of the gamma transcripts were small compared to published intestinal **TCR** delta recombinations. All CDR3 regions contained at least one charged amino acid. The limited number of functional transcripts adds evidence to the oligoclonality of intestinal **TCRs** expressing the **TCR** V gamma (I) family. The short CDR3 regions support the concept of limited antigen recognition by this lymphocyte population.

AB The majority of human intestinal intraepithelial lymphocytes (HIELS) express CD8+, and the **T cell Receptor** (**TCR**) alpha **beta**. A minority of HIELS utilize **TCR** gamma delta chains. V delta 1 is established as the **TCR**-delta expressed by most **TCR** gamma delta HIELS. Since V delta 1 is the dominant intestinal **TCR** and V gamma (I) family is preferentially used in forming a heterodimer, this study was conducted to characterize individual V. . . . from four samples of colonic epithelium obtained from patients undergoing colon resection or endoscopy. RNA was isolated and cDNA synthesized. **PCR** amplification was performed with **consensus** J gamma and V gamma **primers** in these regions. **PCR** products were cloned and sequenced. All samples had V gamma 4 transcripts, a majority V gamma 3 whereas V gamma 2 and V gamma 8 were less frequent. No V gamma 2 transcripts had any predicted **TCR** protein products. Similarly, very few potentially productive V gamma 3 transcripts were found. In contrast, almost all V gamma 4. . . . only V gamma 8 transcript was in-frame. The CDR3 region of the gamma transcripts were small compared to published intestinal **TCR** delta recombinations. All CDR3 regions contained at least one charged amino acid. The limited number of functional transcripts adds evidence to the oligoclonality of intestinal **TCRs** expressing the **TCR** V gamma (I) family. The short CDR3 regions support the concept of limited antigen recognition by this lymphocyte population.

L14 ANSWER 15 OF 23 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96026058 MEDLINE
DOCUMENT NUMBER: 96026058 PubMed ID: 7572791
TITLE: Correlation between presence of clonal rearrangements of immunoglobulin heavy chain genes and B-cell antigen expression in Hodgkin's disease.
AUTHOR: Orazi A; Jiang B; Lee C H; English G W; Cattoretti G; John K; Neiman R S
CORPORATE SOURCE: Division of Hematopathology, Indiana University School of Medicine, Indianapolis, USA.
SOURCE: AMERICAN JOURNAL OF CLINICAL PATHOLOGY, (1995 Oct) 104 (4) 413-8.
Journal code: 3FK; 0370470. ISSN: 0002-9173.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19980206
Entered Medline: 19951121

AB Southern blot analysis of Hodgkin's disease (HD), although often compromised by the small number of abnormal cells present in the tissue, have tended to favor a B-cell derivation of the Hodgkin's and Reed-Sternberg (HRS) cells in cases of nodular sclerosis (NS) and mixed cellularity (MC) Hodgkin's disease. Eighteen frozen and 29 paraffin-embedded sections of lymph node specimens from 29 patients with pretreatment HD (22 NSHD and 7 MCHD) were studied by molecular analysis and immunohistochemistry to determine the phenotype of HRS cells. All cases were reviewed and showed typical morphology and CD45-, CD30+, CD15+, BLA.36+ HRS cells. In 11 of 29 (38%) cases, HRS cells were reactive with at least one B-cell marker (CD20, CD79a, MB2), 7 of 29 (24%) cases showed reactivity with the T-cell marker CD3, and 11 of 29 (38%) cases displayed a "null" phenotype. By using a polymerase chain reaction (**PCR**) and **consensus primers** for the V and J regions of the immunoglobulin heavy chain (IgH) gene, the authors were able to detect B-cell clonality in 9 of 18 (50%) frozen samples of HD analyzed. IgH gene rearrangement was present in 8 of 15 (53%) NSHD and in 1 of 3 (33%) MCHD. In five of nine (56%) of these cases, HRS cells were reactive with at least one B-cell marker, whereas one case expressed the T-cell marker CD3. The other three cases with IgH gene rearrangement showed a "null" immunophenotype. IgH gene analysis was negative in all remaining CD3+ cases and in two other cases that expressed B-cell markers by immunohistology. Southern blotting failed to detect rearrangement of the **T-cell receptor beta**-chain gene and immunoglobulin heavy and light genes in any of these cases. The results show that **PCR** represents a specific and sensitive technique for the detection of IgH gene rearrangements in cases of Hodgkin's disease. The results also suggest a lymphoid B-cell derivation of HRS cells in a high proportion of the cases.

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consensus primers for the V and J regions of the immunoglobulin heavy chain (IgH) gene, the authors were able to detect B-cell. . . cases and in two other cases that expressed B-cell markers by immunohistology. Southern blotting failed to detect rearrangement of the **T-cell receptor beta**-chain gene and immunoglobulin heavy and light genes in any of these cases. The results show that **PCR** represents a specific and sensitive technique for the detection of IgH gene rearrangements in cases of Hodgkin's disease. The results. . .

L14 ANSWER 16 OF 23 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 95369847 MEDLINE
DOCUMENT NUMBER: 95369847 PubMed ID: 7642232
TITLE: Identification and characterization of T-cell antigen receptor-related genes in phylogenetically diverse vertebrate species.
AUTHOR: Rast J P; Haire R N; Litman R T; Pross S; Litman G W
CORPORATE SOURCE: University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: RO1AI23338 (NIAID)
SOURCE: IMMUNOGENETICS, (1995) 42 (3) 204-12.
Journal code: GI4; 0420404. ISSN: 0093-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U22666; GENBANK-U22667; GENBANK-U22668; GENBANK-U22669; GENBANK-U22670; GENBANK-U22671; GENBANK-U22672; GENBANK-U22673; GENBANK-U22674; GENBANK-U22675; GENBANK-U22676; GENBANK-U22677; GENBANK-U22678; GENBANK-U22679; GENBANK-U23067
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19950930
Entered Medline: 19950920

AB Characterization of the structure, multiplicity, organization, and cell lineage-specific expression of **T-cell receptor** (**TCR**) genes of nonmammalian vertebrate species is central to the understanding of the evolutionary origins of rearranging genes of the vertebrate immune system. We recently described a polymerase chain reaction (**PCR**) strategy that relies on short sequence similarities shared by nearly all vertebrate **TCR** and immunoglobulin (Ig) variable (V) regions and have used this approach to isolate a **TCR beta** (TCRB) homolog from a cartilaginous fish. Using these short **PCR** products as probes in spleen cDNA and genomic libraries, we were able to isolate a variety of unique **TCR** and **TCR**-like genes. Here we report the identification and characterization of a chicken **TCR** gamma (TCRG) homolog, apparent Xenopus and pufferfish **TCR** alpha (TCRA) homologs, and two horned shark **TCR** delta (TCRD)-like genes. In addition, we have identified what could be a novel representative of the Ig gene superfamily in the pufferfish. This method of using short, minimally **degenerate PCR primers** should speed progress in the phylogenetic investigations of the **TCR** and related genes and lend important insights into both the origins and functions of these unique gene systems.

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L14 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 12
ACCESSION NUMBER: 1995:971124 CAPLUS
DOCUMENT NUMBER: 124:46784
TITLE: A rapid and reliable PCR method for detecting clonal T cell populations
AUTHOR(S): Lynas, C; Howe, D; Copplestone, JA; Johnson, SAN; Phillips, MJ
CORPORATE SOURCE: Department Haematology, Derriford Hospital, Plymouth, PL6 8DH, UK
SOURCE: Clin. Mol. Pathol. (1995), 48(2), M101-M104
CODEN: CMPAFI; ISSN: 1355-2910
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim was to establish a reverse transcription polymerase chain reaction (RT-**PCR**) for the detection of clonal T cell populations, and to evaluate the sensitivity and reliability of the technique. After reverse transcription of the target RNA with a **consensus T cell receptor** (**TCR**) .**beta**. const. (C) region **primer**, **consensus** C, variable (V), diversity (D) and joining (J) region **primers** were used to amplify across various portions of the **TCR**.**beta**. V-D-J-C junction. In normal T cells the polyclonal rearrangements produce a ladder of **PCR** bands representing the different sized junction fragments. The presence of a T cell clone leads to over-representation of one junction fragment, hence a disproportionately brighter band in the **PCR** ladder. In a series of 16 patients the RT-**PCR** detected nine of nine shown to have a clonal **TCR**.**beta**. rearrangement by Southern blotting and for six of seven patients, it confirmed the presence of a clone indicated by histol. or immunophenotyping with FACS anal., but which was undetectable (five patients) or not investigated (two patients) by Southern blotting. Investigations mixing RNA from normal lymphocytes and the Jurkat **TCR**-V.**beta**.8 T cell line suggested that the method was more sensitive than Southern blotting. All **PCR** methods are

faster and easier than Southern blotting, but RT-**PCR** also improves detection of clonal T cell populations, is reliable and produces results that are easy to interpret.

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L14 ANSWER 18 OF 23 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 95023888 MEDLINE
DOCUMENT NUMBER: 95023888 PubMed ID: 7937749
TITLE: T-cell receptor gene homologs are present in the most primitive jawed vertebrates.
AUTHOR: Rast J P; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701.
CONTRACT NUMBER: AI-23338 (NIAID)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Sep 27) 91 (20) 9248-52. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U07622; GENBANK-U07623; GENBANK-U07624; GENBANK-U09531; GENBANK-U09532; GENBANK-U09533; GENBANK-U09534
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19960129
Entered Medline: 19941027

AB The phylogenetic origins of T-cell immunity and T-cell antigen receptor (**TCR**) genes have not been established. A **PCR** approach using short, minimally **degenerate** oligodeoxynucleotide **primers** complementing conserved variable region segments amplifies **TCR**-like products from the genomic DNA of Heterodontus francisci (horned shark), a representative phylogenetically primitive cartilaginous fish. One of these products has been used as a probe to screen a Heterodontus spleen cDNA library and a clone was identified that is most related at the nucleotide sequence and predicted peptide levels to higher vertebrate **TCR beta**-chain genes. Genomic analyses of the **TCR** homologs indicate that recombining variable and joining region segments as well as constant region exons are encoded by extensive gene families, organized in the multicluster form, characteristic of both the immunoglobulin heavy- and light-chain gene loci in the cartilaginous fishes. Greater numbers of homologous products were identified when a probe complementing the putative constant region of the **TCR** homolog was used to screen the same cDNA library. A high degree of intergenic variation is associated with the putative variable region segments of these isolates. Direct evidence is presented for **TCR** -like genes, which presumably are associated with T-cell function, at the earliest stages in the phylogenetic emergence of jawed vertebrates.

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L14 ANSWER 19 OF 23 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 94179857 MEDLINE
DOCUMENT NUMBER: 94179857 PubMed ID: 7510755
TITLE: A **consensus** primer to amplify both alpha and beta chains of the human T cell receptor.
AUTHOR: Moonka D; Loh E Y
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania Medical Center, Philadelphia.
CONTRACT NUMBER: AI33214 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1994 Feb 28) 169 (1) 41-51. Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19960129
Entered Medline: 19940418

AB The use of reverse transcriptase in conjunction with the polymerase chain reaction (RT-PCR) has proven invaluable in the analysis of the **T cell receptor** (TCR) repertoire of different populations of T cells. However, the presence of a variable region in the **T cell receptor** has hindered the design of **primers** for the 5' end of the **TCR** cDNA. We describe the design and use of a **degenerate consensus primer** that allows amplification of both the alpha and **beta** chains of the human **TCR**. We have used this **primer** in the analysis of the **TCR** distribution of T cell clones, peripheral blood lymphocytes and lymphocytes residing in tissue. In addition, the **primer** has allowed the identification of an alternative splice site in the **beta** chain constant region which cannot translate into a functional constant region. We have found the **primer** to be easy to use, sensitive and specific.

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CT . . . Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Alternative Splicing: GE, genetics
Amino Acid Sequence
Base Sequence
Blotting, Southern
Clone Cells
***Consensus Sequence**
*DNA Primers
DNA, Complementary: BI, biosynthesis
Electrophoresis, Agar Gel
*Gene Amplification
Mice
Molecular Sequence Data
*Polymerase Chain Reaction: MT,. . .

L14 ANSWER 20 OF 23 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:270260 BIOSIS
DOCUMENT NUMBER: PREV199396000485
TITLE: Molecular cloning of major histocompatibility complex class I cDNAs from Atlantic salmon (Salmo salar.
AUTHOR(S): Grimholt, Unni Vvar Hordvik (1); Fosse, Viggo M.; Olsaker, Ingrid; Endresen, Curt; Lie, Oystein
CORPORATE SOURCE: (1) Dep. Animal Genetics, Norwegian College of Vet. Med., P.O. Box 8146 Dep., N-0033 Oslo 1 Norway
SOURCE: Immunogenetics, (1993) Vol. 37, No. 6, pp. 469-473. ISSN: 0093-7711.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The major histocompatibility complex (Mhc) has attracted much attention because of its immense polymorphism, its importance in transplantation, and its indisputable role in disease susceptibility in humans (Chen and Parham 1989; Hill et al. 1991) and in animals (Lie 1990). Previously, typical Mhc features reflected in allograft rejection and mixed leucocyte reactivity were the only indications that an Mhc also existed in teleost fish (Stet and Egberts 1991). The use of polymerase chain reaction (**PCR**) with **degenerate** oligonucleotides from conserved Mhc regions provided the first direct evidence for Mhc class I and class II genes in a fish, the teleost carp (Hashimoto et al. 1990). The primary aim of our study was to isolate and characterize expressed Mhc molecules in Atlantic salmon, and thereby provide data for further studies on evolutionary and disease aspects of the Mhc and its polymorphism. An atlantic salmon-specific Mhc probe from leucocyte RNA was generated by **PCR** based on **primers** from conserved regions of known Mhc genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik and co-workers (this issue). This salmon-specific probe was employed to screen a leucocyte lambda-gt10 cDNA library based on a few individuals, from which Mhc-positive cDNAs were derived. The cDNAs analyzed in this report were established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal **primers**, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using the UWGCG software (Devereux et al. 1984). The FASTA program (Pearson and Lipman 1988) was used to search the EMBL database. In accordance with the nomenclature proposed by Klein and co-workers (1990), we adopted the designation Mhc-Sasa, as proposed by Stet and Egberts (1991), for the two partial Atlantic salmon (Salmo salar) Mhc nucleotide sequences which we aligned to the EMBL database. One of these clones, p18, shared sequence similarity to Mhc class II molecules (Hordvik et al., this issue). The other clone, p23 (1.8 kilobase (kb)), showed sequence similarity to Mhc class I sequences with a non-translated tail of 1200 nucleotides (nt) and an open reading frame (orf) of 190 aminoacids (aa) starting in the middle of the alpha-2 domain (Fig. 1). The latter cDNA clone was used in a second screening of the cDNA library, which resulted in a potential full-length clone, Sasa p30 (2.8 kb), with an orf corresponding to 343 aa and a nontranslated tail of 1800 nt (Fig. 1). The domain boundaries of Sasa p30 were assigned by alignment with other Mhc class I molecule (Fig. 2). The aa sequence similarities between Sasa and Xenopua, and lizard, man, mouse, chicken, and carp are striking, and support the hypothesis that the isolated cDNA clones encode salmon Mhc class I molecules. Both and cysteines forming intrachain disulphide bonds within the alpha-2 and alpha-3 domains, and the potential glycosylation site at N-84 (numbering is based on the salmon sequence), are conserved. In the putative Sasa p30 transmembrane region there is a stretch of 21 hydrophobic residues flanked on both sides by hydrophilic segments, indicating a membrane anchored protein. Most of the residues assumed to be directly involved in the structure of the alpha-3 domain are conserved in the salmon sequence (C-198, F-203, Y-204, P-205, W-212, G-234, Y-254, C-256, and V-258; Williams et al. 1987). Nine residues pointing into the antigenic recognition site, and probably involved in recognizing constant features

on processed antigens, are conserved in the alpha-1 and alpha-2 domains of humans and mice (Bjorkman et al. 1987). These residues are also conserved in the salmon sequence (L-5, Y-7, F-21, G-25, Y-57, T-140, K-143, Y-157, and Y-169). The signal peptide may be incomplete, as the cDNA clone started with a methionine residue. Both cDNA clones contained 17 repeated CA dinucleotides 110 nt after the first stop codon. This repeated sequence is polymorphic (data will be presented elsewhere), and can be used as an Mhc-linked marker. The two Sasa clones, p23 and p30, differed by 24 nt representing 14 aa residues (Fig. 1). Eleven of the variable aa positions resided in the alpha-2 helical domain and only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human **T-cell receptor** interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only one substitution corresponded to a human, polymorphic, peptide-binding residue (res. 154). It is not possible to determine from our data whether the p23 and p30 cDNA clones are alleles or originate from different genes (isotypes). However, the clustering of replacement substitutions in the alpha-2 region, and the fact that the library from which the cDNA clones were selected was derived from several individuals, supports the hypothesis that the observed variation is attributable to allelism. An amino acid comparison between the salmon alpha domains and those of carp, chicken, HLA-A, H-2K, and lizard showed the significantly lowest similarity to carp (p lt 0.05). The low similarity between salmon and carp is also reflected in the phylogenetic tree (Fig. 3) based on the membrane-proximal aa sequences of Mhc class I (alpha-3) and class II (alpha-2 and **beta**-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is jointed to the H-2K/HLA-A node, but this is a doubtful result. Similarly, the evolutionary relationship between carp, Xenopus, and shark class I sequences are uncertain, and more Mhc class I sequences from lower vertebrates are needed to clarify the picture. All the class II sequences reside on the same branch. Shark class II is joined to a human class II alpha sequence, and the trout and salmon class II peptides are very similar and branched together with carp **beta**-2. Hashimoto and co-workers (1990) used **degenerate primers** directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast to the carp class II sequence, originates from a pseudogene and has thus acquired a considerable number of mutations. The carp class I sequence could also represent a nonclassical carp Mhc molecule. Both suggestions would explain why the carp class I sequence has the lowest overall alpha domain aa similarity (20%) to salmon. Further speculation on teleostean evolution must be deferred until further information is available on expressed carp Mhc class I sequences. A FASTA search with the p30 cDNA sequence identified 40 Mhc class I sequences as being most similar to the salmon sequence. These sequences included both nonclassical (mouse Q7(b), mouse T1a(c), and human HLA-G (HLA 6.0)) and classical Mhc class I genes. The question as to whether Atlantic salmon has both classical and nonclassical homologues, as seen in human and mouse, will be possible to answer when more Sasa loci have been identified. In conclusion, this study, together with the work done by Hordvik and co-workers (this issue), demonstrates the existence of expressed Mhc class I and class II molecules in Atlantic salmon. The clonal variation seen in these reports indicates allelic polymorphism as seen in other species, but the number of alleles and loci involved remains to be established. The teleost class II **beta**-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides is unclear. Further information on expressed carp class I sequences is needed to resolve this.

AB. . . only indications that an Mhc also existed in teleost fish (Stet and Egberts 1991). The use of polymerase chain reaction (**PCR**) with **degenerate** oligonucleotides from conserved Mhc regions provided the first direct evidence for Mhc class I and class II genes in a. . . and disease aspects of the Mhc and its polymorphism. An atlantic salmon-specific Mhc probe from leucocyte RNA was generated by **PCR** based on **primers** from conserved regions of known Mhc genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik. . . established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal **primers**, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using. . . only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human **T-cell receptor** interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only. . . phylogenetic tree (Fig. 3) based on the membrane-proximal aa sequences of Mhc class I (alpha-3) and class II (alpha-2 and **beta**-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is jointed. . . class II alpha sequence, and the trout and salmon class II peptides are very similar and branched together with carp **beta**-2. Hashimoto and co-workers (1990) used **degenerate primers** directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast. . . seen in other species, but the number of alleles and loci involved remains to be established. The teleost class II **beta**-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides. . .

L14 ANSWER 21 OF 23 MEDLINE DUPLICATE 15

ACCESSION NUMBER:	93381275 MEDLINE
DOCUMENT NUMBER:	93381275 PubMed ID: 8396607
TITLE:	Transformation of mycosis fungoides: T-cell receptor beta gene analysis demonstrates a common clonal origin for plaque-type mycosis fungoides and CD30+ large-cell lymphoma.
AUTHOR:	Wood G S; Bahler D W; Hoppe R T; Warnke R A; Sklar J L; Levy R
CORPORATE SOURCE:	Department of Dermatology, Case Western Reserve University, Cleveland, Ohio.
CONTRACT NUMBER:	AR40844 (NIAMS) CA34233 (NCI)
SOURCE:	JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1993 Sep) 101 (3) 296-300. Journal code: IHZ; 0426720. ISSN: 0022-202X.
PUB. COUNTRY:	United States Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199310
ENTRY DATE:	Entered STN: 19931029

Last Updated on STN: 19931029
Entered Medline: 19931012

AB It is well recognized that patients with classical mycosis fungoides (MF) may develop a large-cell lymphoma (LCL), a phenomenon known as "transformation." An unresolved issue regarding the transformation of MF is whether MF and LCL represent two separate lymphomas or whether they are derived from the same T-cell clone. We report the clinicopathologic, immunophenotypic, and immunogenotypic analysis of MF and LCL in a white male. He developed a rash at age 51 that was diagnosed at age 56 as clinical stage IA patch/plaque MF. After topical nitrogen mustard and total skin electron beam therapy for progressive generalized CD3+CD4+ patch/plaque lesions, he developed nodules of Ki-1+ (CD30+) T-LCL at age 72. Southern blot analysis of DNA digested with Bg/II or BamHI and probed with a **T-cell receptor** (TCR)-**beta** gene J **beta** 1/J **beta** 2 probe showed a single, identical rearranged band in both the MF and LCL skin lesions that had been obtained 4 years apart. V **beta** gene family--specific gene amplification assays demonstrated dominant V **beta** 6 **PCR** products in both types of lesions. These **PCR** products and lesional cDNA exhibited a monoclonal pattern when amplified with **consensus TCR-beta** gene VDJ joint **primers** and electrophoresed under conditions that allowed the resolution of small differences in size. Furthermore, sequence analysis of the V **beta** 6 **PCR** products amplified from both the MF and LCL lesions showed an identical nucleotide sequence involving V **beta** 6.4, D **beta** 1.1, J **beta** 1.2, and C **beta** 1. These findings indicate that both the MF and the LCL in this patient arose from the same T-cell clone and that these diseases developed at a stage in the clone's differentiation subsequent to rearrangement of the **TCR-beta** gene.

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L14 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:606319 CAPLUS
DOCUMENT NUMBER: 117:206319
TITLE: Identification of cell subpopulations using modified PCR to amplify DNA encoding proteins with constant and variable regions
INVENTOR(S): Danska, Jayne S.; Fathman, Garrison C.
PATENT ASSIGNEE(S): Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9119816	A1	19911226	WO 1991-US4317	19910617
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2086015	AA	19911221	CA 1991-2086015	19910617

PRIORITY APPLN. INFO.: US 1990-541123 19900620

AB A method for amplifying DNA encoding a protein having a const. and variable region by a polymerase chain reaction (**PCR**) modification is described. The method employs 2 **primers**, one of which is complementary to a const. region. The other is a **degenerate primer** complementary to a portion of the DNA encoding a **consensus** sequence. The amplified DNA can be cloned and sequenced, so that the cells expressing the protein can be identified. The resulting information can be used to design therapies for autoimmune diseases, lymphomas, and leukemias (no data). This procedure was applied to amplification, cloning, and sequencing of mouse **T-cell receptor** .alpha. and **.beta.** cDNA fragments comprising V and J regions.

AB A method for amplifying DNA encoding a protein having a const. and variable region by a polymerase chain reaction (**PCR**) modification is described. The method employs 2 **primers**, one of which is complementary to a const. region. The other is a **degenerate primer** complementary to a portion of the DNA encoding a **consensus** sequence. The amplified DNA can be cloned and sequenced, so that the cells expressing the protein can be identified. The resulting information can be used to design therapies for autoimmune diseases, lymphomas, and leukemias (no data). This procedure was applied to amplification, cloning, and sequencing of mouse **T-cell receptor** .alpha. and **.beta.** cDNA fragments comprising V and J regions.

L14 ANSWER 23 OF 23 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 91184261 MEDLINE
DOCUMENT NUMBER: 91184261 PubMed ID: 2009906
TITLE: Conserved nucleotide sequences at the 5' end of T cell receptor variable genes facilitate polymerase chain reaction amplification.
AUTHOR: Broeren C P; Verjans G M; Van Eden W; Kusters J G; Lenstra J A; Logtenberg T
CORPORATE SOURCE: Institute of Infectious Diseases and Immunology, School of Veterinary Medicine, University of Utrecht, The Netherlands.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Mar) 21 (3) 569-75.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19910526
Entered Medline: 19910503

AB Alignment of all available nucleotide sequences of mouse and rat alpha/**beta T cell receptor** (**TcR**) variable (V) regions revealed the presence of relatively conserved sequences at the 5' end of the V gene segments. Based on these conserved sequences, **degenerate primers** were developed for use in the polymerase chain reaction (**PCR**). The **degenerate primers** developed on the basis of the conserved sequences at the 5' end of rat and mouse V gene segments are expected to enable the amplification of all mouse and rat **TcR** alpha/**beta** chain V regions. To test their applicability, the **primers** were used for the amplification of the V region of the **TcR** alpha/**beta** expressed by rat T cell lines. After amplification, the **TcR** V regions expressed were cloned and sequenced. The Z1a T cell line was shown to use the same **TcR** V gene segments (V alpha 2 and V **beta** 8.2), as most other experimental allergic encephalomyelitis associated T cell lines, but had different D and J segments. In spite of these differences at the nucleotide level, a remarkable conservation of the amino acid sequence at the V **beta** D **beta** J **beta** junction was found. Alignment of a large number of human V alpha and V **beta** gene segments revealed the presence of similarly conserved sequences. **Degenerate primers** based on these conserved sequences enabled the amplification of **TcR** V regions of human T cell lines.

AB Alignment of all available nucleotide sequences of mouse and rat alpha/**beta T cell receptor** (**TcR**) variable (V) regions revealed the presence of relatively conserved sequences at the 5' end of the V gene segments. Based on these conserved sequences, **degenerate primers** were developed for use in the polymerase chain reaction (**PCR**). The **degenerate primers** developed on the basis of the conserved sequences at the 5' end of rat and mouse V gene segments are expected to enable the amplification of all mouse and rat **TcR** alpha/**beta** chain V regions. To test their applicability, the **primers** were used for the amplification of the V region of the **TcR** alpha/**beta** expressed by rat T cell lines. After amplification, the **TcR** V regions expressed were cloned and sequenced. The Z1a T cell line was shown to use the same **TcR** V gene segments (V alpha 2 and V **beta** 8.2), as most other experimental allergic encephalomyelitis associated T cell lines, but had different D and J segments. In spite of these differences at the nucleotide level, a remarkable conservation of the amino acid sequence at the V **beta** D **beta** J **beta** junction was found. Alignment of a large number of human V alpha and V **beta** gene segments revealed the presence of similarly conserved sequences. **Degenerate primers** based on these conserved sequences enabled the amplification of **TcR** V regions of human T cell lines.

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=> s kay R?/au
L15       2394 KAY R?/AU

=> s l15 and TCR and PCR
L16          1 L15 AND TCR AND PCR

=> dis l16 ibib abs kwic
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L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:795052 CAPLUS
DOCUMENT NUMBER: 130:37286
TITLE: Immunological method
INVENTOR(S): **Kay, Richard Andrew**
PATENT ASSIGNEE(S): University of Dundee, UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854223	A2	19981203	WO 1998-GB1382	19980527
WO 9854223	A3	19990304		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9876631	A1	19981230	AU 1998-76631	19980527
AU 728909	B2	20010118		
EP 1017724	A2	20000712	EP 1998-924427	19980527

R: CH, DE, FR, GB, IT, LI, NL, SE

PRIORITY APPLN. INFO.:	GB 1997-10820	A	19970527
	WO 1998-GB1382	W	19980527

AB A method of identifying an antigen-responsive T cell within a population of T cells, the method comprising the steps of: (1) obtaining a sample contg. T cells which have responded to the antigen; (2) detg. individually for each of a plurality of specific T cell receptors, or individually for each of a plurality of subsets of T cell receptors, whether expression of a gene encoding a specific T cell receptor, or whether expression of genes encoding a subset of T cell receptors, has increased per specific T cell receptor-pos. T cell or per specific T cell receptor-pos. T cell subset compared to the expression of said gene or genes in a sample contg. T cells which have not responded to the antigen. The method is useful for identifying antigen-responsive T cells which are assocd. with a disease state such as rheumatoid arthritis.
IN **Kay, Richard Andrew**
ST **TCR** antigen T cell rheumatoid arthritis
IT Genes (animal)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**TCR** subsets; detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with

antigen-responsive T cells)
IT RT-**PCR** (reverse transcription-polymerase chain reaction)
(competitive; detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)
IT Allergies
Autoimmune diseases
Graft vs. host reaction
Immunological diseases
Infection
PCR (polymerase chain reaction)
Rheumatoid arthritis
Sjogren's syndrome
T cell (lymphocyte)
Transplant rejection
Tumors (animal)
Vaccines
(detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)
IT CD28 (antigen)
Staphylococcal enterotoxin B
Toxic shock syndrome toxin 1
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)
IT Superantigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)
IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)
IT Antibodies
mRNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)
IT **TCR** (T cell receptors)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); USES (Uses)
(subsets; detn. of **TCR** subsets or their gene expression for identification of and diagnosis of diseases assocd. with antigen-responsive T cells)

=> s l15 and TCR
L17 32 L15 AND TCR

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18 18 DUP REM L17 (14 DUPLICATES REMOVED)

=> dis l18 1-18 ibib abs

L18 ANSWER 1 OF 18 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000429067 MEDLINE
DOCUMENT NUMBER: 20384795 PubMed ID: 10925285
TITLE: Antigen triggering selectively increases TCRBV gene transcription.
AUTHOR: Lennon G P; Sillibourne J E; Furrie E; Doherty M J; **Kay R A**
CORPORATE SOURCE: Department of Molecular and Cellular Pathology, University of Dundee, Ninewells Hospital and Medical School, Dundee, United Kingdom.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Aug 15) 165 (4) 2020-7.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914
AB When the **TCR** binds Ag it is phosphorylated, internalized, and degraded. We wished to examine whether this process was accompanied by a specific concomitant increase in **TCR** mRNA levels. To do this, PBMC and a T cell clone were cultured with a series of superantigens and an alloantigen. Only T cells specifically responding to an antigenic stimulus had increased levels of **TCR** beta-chain variable (TCRBV)-specific mRNA. This response was apparent after 48 h, peaked around 72 h, and was still elevated after 7 days. Increased gene transcription appeared to be driven solely by Ag as specific Ag depletion prevented culture supernatants transferring this effect. The level of TCRBV mRNA elevation was not influenced by the stimulating Ag, but appeared dependent on the gene encoding the stimulated **TCR**. Reporter gene assays, using cloned TCRBV gene promoters, confirmed both that **TCR** gene transcription rises after stimulation and that basal and stimulated levels of **TCR** transcription vary between different TCRBV genes. These data conclusively demonstrate that there is no direct relationship between TCRBV mRNA and T cell number, and that future repertoire studies must take both factors into account.

L18 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:226584 CAPLUS
DOCUMENT NUMBER: 130:236324
TITLE: Sequence analysis of DA and Sprague Dawley rat T-cell receptor .beta.-chain promoters. [Erratum to document cited in CA130:109050]
AUTHOR(S): Sillibourne, James E.; **Kay, Richard A.**

CORPORATE SOURCE: Dep. Molecular and Cellular Pathology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
SOURCE: Immunogenetics (1999), 49(3), 246
CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Figs. 1 and 2 of this Sequence Register article were incorrect as originally printed; the correct versions are given.

L18 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:154413 BIOSIS
DOCUMENT NUMBER: PREV200000154413
TITLE: The duodecamer motif is critical for both basal and stimulated TCRBV promoter function.
AUTHOR(S): Doherty, M. J. (1); Lennon, G. P. (1); Sillibourne, J. E. (1); Furrie, E. (1); **Kay, R. A. (1)**
CORPORATE SOURCE: (1) Dept. Molecular and Cellular Pathology, University of Dundee, Dundee, DD1 9SY UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 123. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L18 ANSWER 4 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:139956 BIOSIS
DOCUMENT NUMBER: PREV200000139956
TITLE: The TCRBV13 **TCR** repertoire in anti-52 KDA Ro autoantibody-positive Sjogren's syndrome.
AUTHOR(S): Furrie, E. (1); Doherty, M. J. (1); Kershaw, A.; Crighton, A. J.; Morley, K.; **Kay, R. A. (1)**
CORPORATE SOURCE: (1) Dept. Molecular and Cellular Pathology, University of Dundee, Dundee, DD1 9SY UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 33. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy and Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy and Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L18 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:795052 CAPLUS
DOCUMENT NUMBER: 130:37286
TITLE: Immunological method
INVENTOR(S): **Kay, Richard Andrew**
PATENT ASSIGNEE(S): University of Dundee, UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854223	A2	19981203	WO 1998-GB1382	19980527
WO 9854223	A3	19990304		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876631	A1	19981230	AU 1998-76631	19980527
AU 728909	B2	20010118		
EP 1017724	A2	20000712	EP 1998-924427	19980527
R: CH, DE, FR, GB, IT, LI, NL, SE				

PRIORITY APPLN. INFO.: GB 1997-10820 A 19970527
WO 1998-GB1382 W 19980527

AB A method of identifying an antigen-responsive T cell within a population of T cells, the method comprising the steps of: (1) obtaining a sample contg. T cells which have responded to the antigen; (2) detg. individually for each of a plurality of specific T cell receptors, or individually for each of a plurality of subsets of T cell receptors, whether expression of a gene encoding a specific T cell receptor, or whether expression of genes encoding a subset of T cell receptors, has increased per specific T cell receptor-pos. T cell or per specific T cell receptor-pos. T cell subset compared to the expression of said gene or genes in a sample contg. T cells which have not responded to the antigen. The method is useful for identifying antigen-responsive T cells which are assocd. with a disease state such as rheumatoid arthritis.

L18 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:683257 CAPLUS
DOCUMENT NUMBER: 130:109050
TITLE: Sequence analysis of DA and Sprague Dawley rat T-cell receptor .beta.-chain promoters
AUTHOR(S): Sillibourne, James E.; **Kay, Richard A.**
CORPORATE SOURCE: Department of Molecular and Cellular Pathology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
SOURCE: Immunogenetics (1998), 48(5), 356-358
CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The genomic sequences of 4 rat **TCR** .beta.-chain genes were analyzed in 1 inbred (DA) and 1 outbred (Sprague Dawley) rat strains. The sequences suggest that these promoters are capable of binding a comprehensive range of lineage-specific and non-lineage-specific factors, including putative binding sites for AP-1, AP-2, Sp1, GATA-binding factors, CREB, Ets-1, LEF-1, AML-1, and TCF-1. CAAT and TATA boxes were

also identified in some of the promoters.
REFERENCE COUNT: 6
REFERENCE(S): (1) Halle, J; Mol Cell Biol 1997, V17, P4220 CAPLUS
(2) Kay, R; Eur J Immunol 1994, V24, P2863 CAPLUS
(3) Li, Y; J Exp Med 1991, V174, P1537 CAPLUS
(5) Rowen, L; Science 1996, V272, P1755 CAPLUS
(6) Smith, L; J Immunol 1991, V147, P375 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:125347 BIOSIS
DOCUMENT NUMBER: PREV199900125347
TITLE: Superantigens increase specific **TCR** gene transcription rates in unseparated human lymphocyte populations.
AUTHOR(S): Lennon, Greig; Sillibourne, James; **Kay, Richard**
CORPORATE SOURCE: Univ. Dep. Molecular Cellular Pathol., Ninewells Hosp. Med. Sch., Dundee DD1 9SY UK
SOURCE: Immunology, (Dec., 1998) Vol. 95, No. SUPPL. 1, pp. 28. Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998 ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 8 OF 18 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97414173 MEDLINE
DOCUMENT NUMBER: 97414173 PubMed ID: 9269034
TITLE: Long-term alloreactive T cell lines and clones express a limited T cell receptor repertoire.
AUTHOR: Tavakol Afshari J; Hutchinson I V; **Kay R A**
CORPORATE SOURCE: School of Biological Sciences, University of Manchester, UK.
SOURCE: TRANSPLANT IMMUNOLOGY, (1997 Jun) 5 (2) 122-8. Journal code: B32; 9309923. ISSN: 0966-3274.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971105
AB Alloreactive T cells recognize either determinants of the intact donor MHC molecules displayed on the surface of transplanted-cells or peptide fragments of donor antigens associated with self-MHC molecules by means of their T cell receptors (**TCR**). To investigate the relationship between the **TCR** beta chain structure and allorecognition, we established and characterized four long-term T cell lines and seven T cell clones derived following a mixed lymphocyte reaction (MLR) between fully histoincompatible DA (RT1a) and LEW (RT1(1)) rat lymph node cells. These DA anti-LEW T cells were phenotypically CD4+, CD8-, alpha beta **TCR** + and produced interferon-gamma but not IL-4, consistent with being Th1 CD4+ T cells. As might be expected, these cells were not significantly cytotoxic and did not display suppressor activity. Analysis of the **TCR** beta chain gene structure revealed a very restricted repertoire in both long-term lines and clones. The TCRBV6S1 gene was present in 15/21 of the alloreactive T cell mRNA transcripts but only 1/12 of unstimulated DA splenic **TCR** mRNA transcripts ($p = 0.0018$). Similarly, the TCRBJ2S1 gene was also used frequently in the alloreactive transcripts (17/21) but in only 2/12 unstimulated splenic transcripts ($p = 0.0013$). Furthermore, all 15 of the alloreactive TCRBV6S1 transcripts had a distinctive four amino acid N region motif not present in any of the unstimulated **TCR** transcripts ($p = 0.0003$). These experiments reveal a distinct homogeneity amongst stable allogeneic T cells in culture. If these results reflect the situation in vivo, the possibility exists that specific immunotherapy may be successful in preventing allograft rejection.

L18 ANSWER 9 OF 18 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96132972 MEDLINE
DOCUMENT NUMBER: 96132972 PubMed ID: 8543797
TITLE: Reduction of early B lymphocyte precursors in transgenic mice overexpressing the murine heat-stable antigen.
AUTHOR: Hough M R; Chappel M S; Sauvageau G; Takei F; **Kay R** ; Humphries R K
CORPORATE SOURCE: Terry Fox Laboratory, British Columbia Cancer Agency, Vancouver, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Jan 15) 156 (2) 479-88. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960227
Last Updated on STN: 19960227
Entered Medline: 19960214
AB To study the role of the murine heat-stable Ag (HSA) in lymphocyte maturation, we generated transgenic mice in which the HSA cDNA was under the transcriptional control of the **TCR** V beta promoter and Ig mu enhancer. The HSA transgene was expressed during all stages of B lymphocyte maturation. Expression was first detected in the earliest lymphoid-committed progenitors, which normally do not express HSA, and subsequently reached the highest levels in pro- and pre-B cells. In bone marrow, the number of IL-7-responsive clonogenic progenitors was < 4% of normal, whereas the frequency of earlier B lymphocyte-restricted precursors, detectable as Whitlock-Witte culture-initiating cells, was normal. Pro- and pre-B cells detected by flow cytometry were reduced by approximately 50% relative to controls. Mature splenic B cells were also reduced but to a lesser extent than in marrow, and their response to LPS stimulation was impaired. Reconstitution of SCID and BALB/c-nu/nu mice with HSA transgenic marrow indicated that the perturbations in B lymphopoiesis were not caused by a defective marrow microenvironment or by abnormal T cells. Our previous studies showed elevated HSA expression throughout thymocyte development, which resulted in a profound depletion of CD4+CD8+ double-positive and single-positive thymocytes. Together, these results indicate that HSA levels can determine the capacity of early T and B lymphoid progenitors to proliferate and survive. Therefore, HSA could serve as an important regulator during the early stages of B and T lymphopoiesis.

L18 ANSWER 10 OF 18 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 96303221 MEDLINE
DOCUMENT NUMBER: 96303221 PubMed ID: 8732480
TITLE: **TCR** gene polymorphisms and autoimmune disease.
AUTHOR: **Kay R A**
CORPORATE SOURCE: Department of Pathology, Ninewells Hospital & Medical School, Dundee, UK.
SOURCE: EUROPEAN JOURNAL OF IMMUNOGENETICS, (1996 Apr) 23 (2) 161-77. Ref: 129
Journal code: AZ6; 9106962. ISSN: 0960-7420.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961022
Last Updated on STN: 19961022
Entered Medline: 19961009

AB Autoimmunity may result from abnormal regulation within the immune system. As the T cell is the principal regulator of the immune system and its normal function depends on immune recognition or self/non-self discrimination, abnormalities of the idiotypic T-cell receptor (**TCR**) may be one cause of autoimmune disease. The **TCR** is a clonally distributed, cell-surface heterodimer which binds peptide antigen when complexed with HLA molecules. In order to recognize the variety of antigens it may possibly encounter, the **TCR**, by necessity, is a diverse structure. As with immunoglobulin, it is the variable domain of the **TCR** which interacts with antigen and exhibits the greatest amount of amino acid variability. The underlying genetic basis for this structural diversity is similar to that described for immunoglobulin, with **TCR** diversity relying on the somatic recombination, in a randomly imprecise manner, of smaller gene segments to form a functional gene. There are a large number of gene segments to choose from (particularly the TCRAV, TCRAJ and TCRBV gene segments) and some of these also exhibit allelic variation. Finally, polymorphisms in non-coding regions of **TCR** genes, leading to biased recombination or expression, are also beginning to be recognized. All these factors contribute to the polymorphic nature of the **TCR**, in terms of both structure and repertoire formation. It follows that inherited abnormalities in either coding or regulatory regions of **TCR** genes may predispose to aberrant T-cell function and autoimmune disease. This review will outline the genomic organization of the **TCR** genes, the genetic mechanisms responsible for the generation of diversity, and the results of investigations into the association between germline polymorphisms and autoimmune disease.

L18 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:384429 BIOSIS
DOCUMENT NUMBER: PREV199598398729
TITLE: Limited heterogeneity of **TCR** V-beta gene utilisation by alloreactive T cells.
AUTHOR(S): Tavakoli, J.; Hutchinson, I. V.; **Kay, R.**
CORPORATE SOURCE: Univ. Manchester, Med. Sch., Manchester M13 9PT UK
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 646. The 9th International Congress of Immunology.
Publisher: 9th International Congress of Immunology San Francisco, California, USA.
Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 12 OF 18 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96023322 MEDLINE
DOCUMENT NUMBER: 96023322 PubMed ID: 7558918
TITLE: A subset of Sjogren's syndrome associates with the TCRBV13S2 locus but not the TCRBV2S1 locus.
AUTHOR: **Kay R A**; Hutchings C J; Ollier W E
CORPORATE SOURCE: Immunology Research Group, University of Manchester, United Kingdom.
SOURCE: HUMAN IMMUNOLOGY, (1995 Apr) 42 (4) 328-30.
Journal code: G9W; 8010936. ISSN: 0198-8859.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951102

AB HGPSS associates with the TCRBV6S7 locus within the **TCR** beta-chain gene complex. However, V beta 6.7 T cells, encoded by this locus, have never been implicated in the salivary gland destruction that characterizes primary Sjogren's syndrome. Both V beta 13 and V beta 2 T cells have been implicated in glandular destruction. We therefore analyzed the association of HGPSS with both TCRBV2S1, the only TCRBV2 locus, and the TCRBV13S2 locus (the TCRBV13 family member which lies closest to TCRBV6S7). Our results show that the prevalence of TCRBV13S2*2 homozygotes is significantly increased in HGPSS and that there is a high degree of linkage disequilibrium between this locus and TCRBV6S7 not previously described across the **TCR** beta-chain gene complex. However, HGPSS does not associate with the TCRBV2S1 locus. These results suggest that it is the V beta 13.2 T cell which may be responsible for the autoimmune destruction that characterizes HGPSS and that the previous association of this condition with the TCRBV6S7 locus is primary due to the linkage disequilibrium that exists between it and TCRBV13S2.

L18 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:204308 CAPLUS
DOCUMENT NUMBER: 122:184945
TITLE: Genetic control of the human V.beta.13.2 T cell repertoire: importance of allelic variation outside the coding regions of the TCRBV13S2 gene
AUTHOR(S): **Kay, Richard A.**; Snowden, Neil; Hajeer, Ali H.; Boylston, Art W.; Ollier, William E. R.
CORPORATE SOURCE: Immunology Research Group, Univ. Manchester, Leeds, UK
SOURCE: Eur. J. Immunol. (1994), 24(11), 2863-7
CODEN: EJIMAF; ISSN: 0014-2980

DOCUMENT TYPE: Journal
LANGUAGE: English
AB In humans, the T cell repertoire is influenced by HLA, T cell receptor null alleles and antigen. Here, the authors describe a novel mechanism, independent of superantigen or T cell receptor structure which influences the T cell repertoire in a V.beta.-dependent manner. The authors have identified a biallelic locus, the TCRBV13S2 T cell receptor gene, where allelic differences predominate in the non-coding regions including transitions, transversions and frameshift deletions. The expressed protein is non-polymorphic at this locus. The TCRBV13S2 genotype profoundly influences the circulating level of V.beta.13.2 CD4 T cells but does not affect T cell receptor expression or function.

L18 ANSWER 14 OF 18 MEDLINE
ACCESSION NUMBER: 95135387 MEDLINE
DOCUMENT NUMBER: 95135387 PubMed ID: 7833889
TITLE: [Idiotypic T-lymphocyte receptor in animal and human autoimmune diseases].
Le recepteur idiotypique des lymphocytes T dans les maladies auto-immunes animales et humaines.
AUTHOR: **Kay R A**; Ollier W E
CORPORATE SOURCE: ACR Epidemiology Research Unit, Manchester, Grande Bretagne, UK.
SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1994) 61 (7-8) 532-45. Ref: 147
Journal code: BQU; 9315664.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950314
Last Updated on STN: 19950314
Entered Medline: 19950227
AB Animal models have demonstrated that the T-cell repertoire is restricted when the response to defined autoantigens is studied. Anti-V beta specific monoclonal antibodies or specific V beta-derived peptides can be used to manipulate autoreactive T-cells to either prevent or treat established experimental disease in animals. In some animal models of arthritis, inherited differences in the **TCR** repertoire can protect against the development of experimental autoimmune disease. Human studies have generally given conflicting results with regard to the role of the **TCR** complexes as susceptibility loci for disease. This may be due to the heterogeneity present in the human population and/or in the diseases studied. In some diseases, where there is convincing evidence for putative autoantigens (multiple sclerosis) or distinct immunodysfunctional pathology (hypergammaglobulinaemic primary Sjogren's syndrome), restricted **TCR** repertoires and germline **TCR** susceptibility loci can be discerned. Recent evidence suggests that autoimmune disease may eventually be mapped to regulatory regions of the **TCR** V genes rather than the allelic differences in coding region structure. This may have implications for the future therapy of autoimmune rheumatic disease.

L18 ANSWER 15 OF 18 MEDLINE
ACCESSION NUMBER: 95135386 MEDLINE
DOCUMENT NUMBER: 95135386 PubMed ID: 7833888
TITLE: [T-lymphocyte receptor genes: genome organization and genetic mechanisms of repertoire diversity].
Genes du recepteur des lymphocytes T: organisation genomique et mecanismes genetiques de la diversite du repertoire.
AUTHOR: **Kay R A**; Ollier W E
CORPORATE SOURCE: ACR Epidemiology Research Unit, Manchester, UK.
SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1994) 61 (7-8) 521-31. Ref: 104
Journal code: BQU; 9315664.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950314
Last Updated on STN: 19950314
Entered Medline: 19950227
AB The T-cell receptor (**TCR**) is fundamental to the immune process in both health and disease. Reviewed here is the genetic organisation of the gene complexes which encode the **TCR** polypeptide chains alpha, beta, gamma, and delta. The **TCR** is by necessity a diverse structure and we consider the genetic mechanisms responsible for this. These include multiple variable gene segment isotypes, somatic recombination of gene segments, imprecisions in the recombination process and allelic variations in gene segments structure and regulation.

L18 ANSWER 16 OF 18 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94298865 EMBASE
DOCUMENT NUMBER: 1994298865
TITLE: Idiotypic T-cell receptor studies in animal and human autoimmune disease.
AUTHOR: **Kay R.A.**; Ollier W.E.R.
CORPORATE SOURCE: ACR Epidemiology Research Unit, Oxford Road,Manchester M13 9PT, United Kingdom
SOURCE: Revue du Rhumatisme (English Edition), (1994) 61/7-8 (470-482).
ISSN: 1169-8446 CODEN: RRHUEX
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB Animal models have demonstrated that the T-cell repertoire is restricted when the response to defined autoantigens is studied. Anti-V.beta. specific monoclonal antibodies or specific V.beta.-derived peptides can be used to manipulate autoreactive T-cells to either prevent or treat established experimental disease in animals. In some animal models of arthritis, inherited differences in the **TCR** repertoire can protect against the development of experimental autoimmune disease. Human

studies have generally given conflicting results with regard to the role of the **TCR** complexes as susceptibility loci for disease. This may be due to the heterogeneity present in the human population and/or in the diseases studied. In some diseases, where there is convincing evidence for putative autoantigens (multiple sclerosis) or distinct immunodysfunctional pathology (hypergammaglobulinaemic primary Sjogren's syndrome), restricted **TCR** repertoires and germline **TCR** susceptibility loci can be discerned. Recent evidence suggests that autoimmune disease may eventually be mapped to regulatory regions of the **TCR** V genes rather than the allelic differences in coding region structure. This may have implications for the future therapy of autoimmune rheumatic disease.

L18 ANSWER 17 OF 18 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94298864 EMBASE
DOCUMENT NUMBER: 1994298864
TITLE: The T-cell receptor genes: Genomic organisation and the genetic basis of repertoire diversity.
AUTHOR: **Kay R.A.**; Ollier W.E.R.
CORPORATE SOURCE: ACR Epidemiology Research Unit, Oxford Road,Manchester M13 9PT, United Kingdom
SOURCE: Revue du Rhumatisme (English Edition), (1994) 61/7-8 (459-469).
ISSN: 1169-8446 CODEN: RRHUEX
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English; French
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L18 ANSWER 18 OF 18 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 91322881 MEDLINE
DOCUMENT NUMBER: 91322881 PubMed ID: 1864006
TITLE: An abnormal T cell repertoire in hypergammaglobulinaemic primary Sjogren's syndrome.
AUTHOR: **Kay R A**; Hay E M; Dyer P A; Dennett C; Green L M; Bernstein R M; Holt P J; Pumphrey R S; Boylston A W; Ollier W E
CORPORATE SOURCE: Regional Immunology Service, St Mary's Hospital, Manchester, UK.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 Aug) 85 (2) 262-4.
Journal code: DD7; 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19910929
Last Updated on STN: 19910929
Entered Medline: 19910911
AB T cell antigen specificity is determined by the products of the genes which encode the variable regions of their receptors. Of the T cell receptor (**TCR**) variable region gene products examined, only V beta 6.7a **TCR**-positive lymphocytes were reduced in primary Sjogren's syndrome patients with IgG1 hypergammaglobulinaemia compared with an age-, sex- and HLA-matched control population. The levels of V beta 6.7a T cells were also significantly reduced when these patients were compared with an age- and sex-matched but HLA-unmatched control group and non-tissue typed normal people of both sexes. Since published studies show no such abnormality in rheumatoid arthritis, systemic lupus erythematosus or other autoimmune diseases, this abnormality may reflect a pathogenic process specific to primary Sjogren's syndrome.

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Williams et al (1992) J. Clinnical Investigation 90:326-333

Beers et al (1993) Journal of leukocyte Biology 54(4):343-350

Arenz et al (1998 Jan) 28(1):70-77

Raju et al (1997 OCt) Journal of Autoimmunity 10(5):479-489

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Roux et al (1996) Human Immunology 48(1-2):135-138

Moonka et al Journal of Immunological Methods (1994) 169(1):41-51

Rast et ak (1997) Immunity 6(1):1-11

Kneba et al (1995) Blood 86(10):3930-3937

Boeren et al (1991) Euroopean Journal of Immunology (1991) 21 (3):569-575

Danska et al (1990) Journal of Experimental Medicine 172(1):27-33

Thank you very much
Amy

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